The Oxford Medicine

BY VARIOUS AUTHORS

VOLUME VIII

EDITED BY

HENRY A CHRISTIAN AM MD LLD ScD (Hon) MACP.,
Hon FRCP (Can), DSM (AMA)

Hersey Professor of the Theory and Practice of Physic Emeritus, Harvard University
Sometime Clinical Professor of Medicine Tufts College Medical School
Sometime Visiting Physician Beth Israel Hospital
Physician in Chief Emeritus, Peter Bent Brigham Hospital, Boston, Mass

NEW YORK
OXFORD UNIVERSITY PRESS

1953

LIBRARY OF CONGRESS CATALOGUE CARD NUMBER 53 5550

PRINTED IN THE UNITED STATES OF AMERICA

MEDICAL TREATMENT OF DISEASE

HENRY A CHRISTIAN A M M D, L L D Sc D (Hon), M A C P, Hon. F R C P (Can) D S M (A M A)

Hersey Professor of the Theory and Practice of Physic, Emeritus, Harvard University, Sometime Clinical Professor of Medicine, Tufts College Medical School, Sometime Visiting Physician, Beth Israel Hospital, Physician in Chief, Emeritus, Peter Bent Brigham Hospital, Boston, Mass

DALE G FRIEND, A B M S M D, F A C P

Colonel, M C, A U S, Southwest Pacific and European Theaters, World War II, Associate in Medicine, Harvard Medical School, Senior Associate in Medicine, Peter Bent Brigham Hospital, Clinical Pharmacologist, Peter Bent Brigham Hospital, Consultant in Medicine, Sturdy Memorial Hospital, Consultant in Medicine, Veterans Administration

MAURICE A SCHNITKER, B S, M D F A C P

Lieut Colonel, M C, A U S Medical Consultant, Pacific Theater, World War II, Director of Medicine, St Vincent's Hospital Senior Attending Physician Toledo Hospital, Chief of Staff, Maumee Valley Hospital Consultant, Toledo State Hospital and Robinwood Hospital, Toledo, Ohio

LIBRARY OF CONGRESS CATALOGUE CARD NUMBER 53 5550

PRINTED IN THE UNITED STATES OF AMERICA

INTRODUCTION

Throughout the ages treatment has been the most difficult and unsatisfactory part of medicine, much of it has been empirical and inexact Beginning with ancient medicine man s impatience for relief from suffering brought about the witches brew and evil tasting bad smelling concoctions And even in the years of enlightenment the fads and fancies of treatment have drawn a degree of approbation and interest from the health seeking masses

Almost from time immemorial thoughtful physicians have opposed the unwarranted use of drugs and procedures And it is interesting that Plato, the famous Greek philosopher and the arch enemy of the purgative treatment joined with physicians in strong condemnation. 'Every disease he said, is akin to the nature of the living being and is only irritated by stimulants' Anticipating the trends of modern medicine, when physicians themselves would be unwilling to submit to promiscuous therapy and to prescribe unholy medication for others he propounded with remarkable insight that on the occasion of an epidemic men fill themselves with waters and winds as if their bodies were a marsh compelling the ingenious sons of Aesculapius to find more names for diseases such as flatulence and catarrh'

Empirical therapy despite the opposition, gradually became a part and parcel of medical practice and facility in writing prescriptions was often the gauge of professional qualifications In time proprietary medicines gutted the shelves of apothecaries and general stores Noting this Sir William Osler with rare understanding and forthrightness, spoke out against empiricism and excessive treatment And while emphasizing the failures he stimulated a deep interest in the basic causes of disease and the true significance of symptoms His associates, Thomas McCrae, H A Lafleur and W S Thayer and a host of pupils took up the cry and gradually false notions were brought to light Courses in therapeutics were modified or replaced with conferences that dealt more logically with simple drugs and intelligent management But as with other progressive movements,

CO EDITORS

BURGESS GORDON, M D

President and William J Mullen Professor of Medicine Woman's Medical College of Pennsylvania, Philadelphia Pennsylvania

WILLIAM J KERR M D

Professor of Medicine University of California Medical School Physician in Chief, University of California Hospital, San Francisco California

CYRUS C STURGIS, M D

Professor of Medicine University of Michigan Director Thomas Henry Simpson Memorial Institute for Medical Research Chairman Department of Internal Medicine, University Hospital, Ann Arbor, Michigan

in stopping such slight continued hematuria a trial period out of bed should be instituted and if blood does not increase in the urine this period may be continued In another case of acute glomerulonephritis, treated at home with a low protein salt poor diet, hospitalization was recommended for studies of increasing nausea During ward rounds it was brought out that continued restriction might be disturbing The patient said I want to eat and enjoy my food Dr Christian asked What do you want to eat? Ham said the patient and ham was ordered with its protein and salt content intact The nausea disappeared promptly and the significance of proper dietary adjustments is related in the text As soon as possible the patient with acute Bright s disease should be given a diet well balanced in carbohydrates, fat and vitamins with 60 to 75 gm of protein, all of which should total 2000 to 2500 calories if the patient is not considerably below average weight

The present textbook on treatment with its loose leaf composition and arrangement for the introduction of new and important information has fulfilled the purposes of the authors A feature of the text is the omission of diagnostic and etiological data that rightfully belong in the textbooks on practice Accordingly the book has become a treatment volume in its own right Both studen and practitioner should gain from the author s vast clinical experience and the fund of knowledge combed from the literature

BURGESS GORDON, M D

PHILADELPHIA PENNSYLVANIA
MAY 1953

the pendulum swung far into the realm of nihilism, and for a time the development of knowledge of therapy was somewhat retarded The attitude of skepticism became the mood of inaction, and in this atmosphere the young physician turned to prepared mixtures and hand me down prescriptions

The concepts of medicine gradually changed from the older notions of structural disease to the functional aspects and thus created a new premise for the introduction of rational treatment and the evaluation of empirical methods With the advent of the antibiotics, hormones vaccines and the accessory food substances, it became apparent to Dr Henry A Christian that treatment called for a companion book for the loose leaf volumes and the standard textbooks of medicine He invited Dr Maurice A Schnitker and Dr Dale G Friend to join with him in writing a book of living therapy Dr Christian drew from his vast experience of academic and hospital medicine Dr Schnitker utilized the unusual opportunities of general practice to elucidate the value of the newer drugs and procedures Close associations in pharmacology and clinical medicine enabled Dr Friend to provide a happy balance of fundamental principles and practical applications in treatment The manuscript was passed from one author to another for criticism and careful integration and was completed before Dr Christian's untimely death

The sections on pulmonary diseases, gastro intestinal conditions, and the cardiovascular system are rich with critical as well as constructive suggestions To illustrate a dictum often expressed in the teachings of Dr Christian — that the value of treatment depends equally on the selection and termination of the regimen — the examples in the section on acute glomerulonephritis are significant They recall the patient who entered the Peter Bent Brigham Hospital after a period of rest in bed for more than three months There had been mild persistent hematuria and hospitalization was requested for an opinion on the need for further bed rest The findings were normal except for the presence of an occasional red blood cell in the urine It was suggested by some at ward rounds, that an additional month in bed might be desirable but the patient posed his own question, 'Do I have to stay in bed the rest of my life? And Dr Christian replied Get into your bathrobe now' Referring to the text on the indications for bed rest in acute glomerulonephritis the authors state 'In some patients small amounts of blood persist in the urine for weeks, after continued bed rest, apparently ineffective

AUTHOR'S PREFACE

This book as the title indicates will describe the treatment including prophylaxis of those diseases or diseased conditions which ordinarily fall in the province of the physician or internist It will not consider those whose treatment usually is carried out by surgeons and specialists Descriptions of a multiplicity of methods of treatment will be avoided When more than one method is described it has been done because the authors believe that not infrequently more than one method should be available to obtain best results since individual patients often show differences in reaction to methods of treatment sometimes one sometimes the other proves more effective

The methods described are those which in the experience of the authors have proved effective or which seem to have had excellent results in the hands of others as reported in their published papers The latter applies in particular to those diseases relatively few in number with which the authors personally have had little clinical experience In very large measure the treatments advised are those which one or all of the authors have observed in use Bibliographic references consist of selected articles most of them covering the past three or four years chosen for their definite value in helping the reader who may wish to secure more information on a specific subject

Methods of treatment will not be presented here simply because they are new The new must have been proved to be better than the old or definitely valuable in addition to the old before it is selected by the authors as a method recommended for use Such proof requires prolonged careful clinical observation by competently trained clinicians of a considerable number of patients with the disease for which the treatment is claimed to be effective No treatment can be judged effective unless a clinical study of it has been made with adequate control observations and the patients under study have undergone prolonged follow up observations Animal experimentation is of great value in many ways to test the use of drugs and other items of treatment before they are used on man but beneficial results

We also wish to acknowledge the great help given to us in the preparation of the manuscript by Dr James Cummins Harriet C Friend Mary Germaine and Virginia Allman

Finally we must insist on taking the opportunity here to thank Mr Russell Garton Miss Margaret Nicholson and Miss Irene Bornemann of the Oxford University Press who were our task masters critics guides and above all our invaluable assistants and faithful friends

H A C
D G F
M A S

The death of Dr Henry A Christian which occurred as this book went to press is noted with sadness We lost not only a co author and distinguished colleague but also a beloved teacher a wise counselor, and a loyal friend

D G F
M A S

BOSTON MASSACHUSETTS
JUNE 1953

on animals and a few patients are not proof that the same treatments will be valuable when applied to large numbers of human beings or even that they will be beneficial rather than injurious Final proof of effectiveness without important toxic reactions must come from controlled observation of patients

The drugs recommended in treatment have been carefully selected for their pharmacological action and chosen from those that are really worth while Official drug terminology is used throughout but in order to avoid confusion common trade names are often given in parentheses after the official term

Treatment rightly should change and often because new methods are being developed rapidly and new drugs are becoming available in large volume Consequently treatment should not be static A book on treatment must be changed frequently either by deletions or by additions A loose leaf book such as this makes changes easy and inexpensive since the purchaser may simply obtain revised pages for insertion into this volume Revisions will be prepared whenever important changes in treatment are found to be clinically worth while

In this book it is assumed that the reader is familiar with existing knowledge of the various aspects of the diseases or diseased conditions other than their treatment and no descriptions of the diseases themselves and their diagnoses are given These will be found in other volumes of *Oxford Medicine* Discussions in this book are limited to the most effective method of treatment *after* the correct diagnosis has been made It is hoped that from them the reader will be able to treat in a satisfactory way patients having any diseases for which treatment is discussed

The authors wish to thank all those who were so helpful to us in the tedious job of writing a book on treatment The advice encouragement and criticism of our many colleagues are gratefully acknowledged We are indebted to Dr Louis I Dublin for permission to use the Tables of Desirable Adult Weights and mortality figures as prepared by the Metropolitan Life Insurance Company and to Dr Joseph H Barach for permission to use his tables of height-weight for children

A great debt of gratitude is owed to the many classes of medical students house officers and residents who through their ever-searching desire to improve their knowledge served to keep us alert to the many changes in this rapidly changing field

We also wish to acknowledge the great help given to us in the preparation of the manuscript by Dr James Cummins Harriet C Friend Mary Germaine and Virginia Allman

Finally we must insist on taking the opportunity here to thank Mr Russell Garton Miss Margaret Nicholson and Miss Irene Bornemann of the Oxford University Press who were our task masters critics guides and above all our invaluable assistants and faithful friends

H A C
D G F
M A S

The death of Dr Henry A Christian which occurred as this book went to press is noted with sadness We lost not only a co author and distinguished colleague but also a beloved teacher a wise counselor, and a loyal friend

D G F
M A S

BOSTON MASSACHUSETTS
JUNE 1953

CONTENTS

PART I

INFECTIOUS DISEASES
GENERAL MEASURES OF TREATMENT

CHAPTER I

NON SPECIFIC MEASURES

In the treatment of infectious diseases various general measures of treatment are indicated These will be described in this section with the understanding that they are to be used in the treatment of all of the infectious diseases with an occasional exception that will be mentioned if such exists when the treatment of each one of the infectious diseases is discussed separately Otherwise it is to be understood that these general measures are to be carried out as an integral part of the treatment of each infectious disease

Isolation

The patient suspected of having an infectious disease should be isolated in a single room until the nature of the disease has been determined If the disease is communicable isolation should be continued Single-room isolation is easiest in application When this is not possible measures to minimize contact directly or through attendants with other individuals well or sick should be instituted These measures consist of the use by those in attendance of protective gowns and coverings for the hair and when infection through the respiratory tract is a possibility of gauze masks frequently changed of placing feeding utensils in very hot preferably boiling, water immediately after use of destroying or sterilizing sputum urine, and feces or promptly disposing of them by sanitarily safe procedures and of using sterilizing methods in cleaning urinals bed

pans, sputum receptacles dishes bed clothes, and other articles used by the patient All persons coming in contact with the patient should wash their hands thoroughly — which includes dipping them in an antiseptic solution such as tincture of benzalkonium (Zephiran) chloride 1 1000, or bichloride of mercury 1 1000 This should be done each time on leaving the patient and before contact with another person If these methods are carefully carried out single room isolation, although desirable is not necessary

Isolation methods such as have been described should be continued well into convalescence Periods of isolation for so called contagious diseases are set by local or state boards of health each physician should familiarize himself with these and see that they are observed Failure to do so may involve the physician in legal difficulty

Where there are special methods of isolation advisable for a given disease they will be described on subsequent pages along with description of treatment advised for that disease

Bed Rest

A patient with an infectious disease should be put to bed if possible in a separate room, or otherwise isolated as described in the previous section He should be kept in bed during the period of fever and for a varying period thereafter the latter depending on the duration of the fever the severity of the illness and the degree of debilitation of the patient When duration of illness is likely to be fairly brief no special forms of bed rest are needed the patient merely lies in bed in any way that is comfortable Most of these patients should be flat in bed If there is dyspnea however they should be propped up by some form of bed rest or by pillows All sicker patients and especially stuporous or sedated ones should be turned in bed at hourly intervals and encouraged to make frequent movement of arms and legs The narrow hospital-type bed on wheels with an arrangement to raise and lower mattress and springs so the patient can easily be put in a sitting or semi reclining position with or without flexing and elevating the legs at the knee, should be used

When the patient has recovered and when in the judgment of the physician recuperation justifies return to some out of bed existence the transition from bed life to normal physical activity should be gradual, passing from the stage of 24 hours in bed through increasing periods of

being propped up in bed and then increasing periods of progression from sitting on the edge of the bed with dangling feet through sitting in a chair near the bed to gradually increasing activity in walking and finally normal physical activity When to make the change from continued bed rest through these progressively increasing activities can be judged by the effect of any of them on the patient's pulse rate If the pulse is greatly accelerated by any of these activities or if it does not return shortly to its previous rate the change has been made too soon or has been too prolonged If this happens a return should be made to what has not caused pulse acceleration and the changes should be carried out more gradually Also if the temperature rises subsequent to these increased activities, return to bed rest is advisable Finally complete convalescence from an infectious disease is not hastened by getting the patient out of bed and on his feet too rapidly On the other hand bed rest can easily be too prolonged this has been the tendency in the past with the consequence of undue invalidism in the patient To go slowly in the early part of the period of convalescence is the wisest procedure for preventing continuing post infectional debility Then return to normal activity should be accelerated in a degree compatible with the patient s debility his physical and psychical make up and his age Infectious diseases vary in duration and debilitating aftereffects Knowledge of this and past experience will be helpful to the physician in planning the patient s transition from bed life to normal activity Wise physicians avoid set rules for the procedures of convalescence

The question always arises how completely the patient should be restricted to bed existence This depends on the physical and mental condition of the patient and his reactions to any physical activity and on the characteristics of the disease from which he is suffering The stuporous patient without dyspnea or the very weak patient does best flat in bed and being turned from side to side or back to side at least hourly Many patients, particularly those with dyspnea however are more comfortable propped up part or all of the time on an efficient bed rest this is desirable particularly at the times for feeding When food or liquids are to be given a nurse should be available to help the stuporous weak or dyspneic patient should be fed by the nurse The nurse is the one who must see that the patient gets the proper amount of food and liquid her insistence can make the difference between the patient s receiving all the desired calories and fluid or his being in a condition of partial starvaton and dehydration

Urination and defecation are important considerations in bed life

pans, sputum receptacles dishes bed clothes, and other articles used by the patient All persons coming in contact with the patient should wash their hands thoroughly—which includes dipping them in an antiseptic solution such as tincture of benzalkonium (Zephiran) chloride 1 1000, or bichloride of mercury 1 1000 This should be done each time on leaving the patient and before contact with another person If these methods are carefully carried out single room isolation although desirable, is not necessary

Isolation methods such as have been described should be continued well into convalescence Periods of isolation for so called contagious diseases are set by local or state boards of health each physician should familiarize himself with these and see that they are observed Failure to do so may involve the physician in legal difficulty

Where there are special methods of isolation advisable for a given disease they will be described on subsequent pages along with description of treatment advised for that disease

Bed Rest

A patient with an infectious disease should be put to bed if possible in a separate room or otherwise isolated as described in the previous section He should be kept in bed during the period of fever and for a varying period thereafter the latter depending on the duration of the fever the severity of the illness and the degree of debilitation of the patient When duration of illness is likely to be fairly brief no special forms of bed rest are needed the patient merely lies in bed in any way that is comfortable Most of these patients should be flat in bed If there is dyspnea, however they should be propped up by some form of bed rest or by pillows All sicker patients and especially stuporous or sedated ones should be turned in bed at hourly intervals and encouraged to make frequent movement of arms and legs The narrow hospital-type bed on wheels with an arrangement to raise and lower mattress and springs so the patient can easily be put in a sitting or semi reclining position with or without flexing and elevating the legs at the knee, should be used

When the patient has recovered and when in the judgment of the physician recuperation justifies return to some out of bed existence the transition from bed life to normal physical activity should be gradual passing from the stage of 24 hours in bed through increasing periods of

be added to the other features of the treatment For this nothing is better than a salicylate such as acetylsalicylic acid (aspirin) 0.3 to 1 gm every 3 or 4 hours but not at night if the patient is sleeping Many prefer to give at the same time a corresponding dose of sodium bicarbonate These drugs should be administered with at least half a glass of water or some other liquid in the patient's dietary Some physicians prefer to use phenacetin in the same way in the same dosage omitting the accompanying sodium bicarbonate Few patients need any additional analgesic drug If they do codeine in 30 or 60 mg doses every 3 hours is preferable, very few need meperidine (Demerol) methadone or morphine although one or another is given all too often

Certain combinations of these drugs are preferred by some physicians to a single one To these may be added caffeine or amphetamine (Benzedrine) as a central nervous stimulant for apprehensive or depressed patients or codeine when there is more pain and greater restlessness The following proprietary combinations are suggested

Empirin Compound given in a dose of 1 tablet every 3 or 4 hours	
acetylsalicylic acid	0.22 gm.
phenacetin	0.16 gm
caffeine	32 mg
Empirin Compound with codeine given in a dose of 1 tablet every 3 or 4 hours.	
acetylsalicylic acid	0.2 7 gm.
phenacetin	0.161 gm
caffeine	32 mg
codeine phosphate	32 mg
Edrisal given in a dose of 1 tablet every 3 or 4 hours.	
acetylsalicylic acid	0.16 gm.
phenacetin	0.16 gm.
amphetamine (benzedrine) sulfate	2.5 mg
Edrisal with codeine given in a dose of 1 tablet every 3 or 4 hours.	
acetylsalicylic acid	0.16 gm.
phenacetin	0.16 gm
amphetamine (benzedrine) sulfate	2.5 mg
codeine	16 mg

For many patients with acute infectious diseases these therapeutic suggestions suffice for the patient's comfort and no sedative or hypnotic drug is needed Other patients however do need a sedative drug particularly a hypnotic for the night hours when sleeplessness makes the patient's general condition less satisfactory and especially when a fairly long period of illness seems probable A mildly hypnotic drug is usually sufficient When the physician decides that such a drug is needed it should be given preferably with a glass of warm milk about a half to an hour before the patient is settled for the night It is a therapeutic error to postpone giving the sedative until a later hour when the patient already has lost needed sleep and probably is growing increasingly rest

Some patients find great difficulty in using urinals or bedpans when flat in bed, and in their struggles use up more energy than they would if aided by a nurse to sit up on the bedpan or to use a bedside commode This is an important individual problem that the physician should decide for each patient who finds it difficult to pass urine or move bowels lying flat in bed Bedpans and bed urinals are far more often overused than underused

The danger of venous thrombosis and possible embolism must be kept constantly in mind especially when the period of bed rest becomes prolonged The danger is lessened by care in preventing dehydration, in avoiding trauma such as may be caused by long periods on the bedpan, and by frequently turning the patient and encouraging body movements, especially of the legs Early recognition of phlebothrombosis or thrombophlebitis by frequent inspection and palpation of the extremities especially the legs, and of pain in the calf by dorsiflexion of the feet (positive Homan's sign) will permit of venous ligation or other appropriate procedures to prevent pulmonary embolism this is very important Heavy sedation may be a factor in causing venous thrombi by inhibiting the patient s moving about The present trend is to over sedate many patients If thrombosis is detected many advise rather than vein ligation, the use of bishydroxycoumarin (Dicumarol) or heparin with dosage of the former checked by prothrombin determinations and of the latter by determination of coagulation time, ligation however, seems preferable for patients with an infectious disease If there are signs of thrombi in the leg veins dicumarol is advised as a measure of prevention when bed rest becomes prolonged, and for stuporous patients

Restlessness and Insomnia

Many patients with infectious diseases are logy and drowsy This is a desirable feature and needs no therapeutic management, even if it is so marked that the patient needs to be aroused for feeding urination, and bowel movements On the other hand some patients are restless, even excited, and are uncomfortable and sleep poorly Some are delirious Many complain of vague aches rather than actual pains Pain is infrequent in patients with acute infectious diseases and when it occurs is rarely severe

When these patients ache, have muscle soreness suffer mild to fairly severe headache or other painful sensations, some drug therapy should

patients are actively delirious however many physicians prefer to use it, giving it in iced fruit juice in doses of 4 to 8 cc repeated at 1 to 2 hour intervals or in still larger doses by rectum once or twice in 24 hours

Diet

All patients with an infectious disease should receive a simple nutritious diet adequate in calories and vitamins The majority need no other dietary regime for their illness is usually of so short a duration that diet is of no great importance For patients with infectious diseases that involve the probability of long duration of fever a high caloric diet, such as that which has been worked out for typhoid fever and which is given on page 89 should be begun as soon as the diagnosis has been made

There is general agreement now that diets for patients with infectious diseases should have the average proportions of protein carbohydrate and fat as far as that is possible in relation to dyspnea difficulty in swallowing and other special conditions in the disease or in the patient, and that these diets should approximate in calorie value those of a normal individual of the same age and size as the patient There should be in the diet at least 1 gm of protein for each kilogram of body weight Food selection should be such that vitamins moderately in excess of normal requirements will be included in the diet This presents no problem if there is variation from day to day in the selected food items which include eggs milk cream and fresh fruit juices For some patients synthetic vitamins should be given in addition to those in the diet This is particularly important in infectious diseases with evidences of liver damage of which infectious hepatitis is a striking example Thiamine is most likely to be deficient a supply of 10 mg of thiamine hydrochloride daily, in addition to the amount that may be in the diet usually suffices

Time for feedings should vary in accordance with the disease and the strength of the patient from 3 meals a day to hourly feedings The majority of these patients do best on a program of 4 or 5 meals a day

The form in which the food is given should depend on the patient s ability or lack of ability to chew thoroughly For the dyspneic or very weak patient all food should be ground up pureed or in liquid form but if the patient can chew with ease food in solid form (so selected as to contain no hard or tough fibrous parts) is more appetizing and the average patient will take more of it

less A mild, quickly acting hypnotic without prolonged action, such as one of the barbiturates is well suited for use in the infectious diseases

It is important to select a barbiturate suited to the needs of the patient and effective for the particular patient during the night with a minimum of after-effect next morning A quickly acting barbiturate whose effect is of relatively short duration is preferable for most of these patients since they have difficulty chiefly in getting to sleep, once asleep they usually sleep satisfactorily through the night For others a longer acting barbiturate is desirable since these patients once asleep, tend to awake and become restless again because they are uncomfortable Each physician learns by trial how to use the barbiturates to obtain the desired effects Since patients differ in their reaction to the various barbiturates he must discover which one is best suited for the particular form of restlessness and insomnia in the specific patient *New and Non official Remedies of the A M A for* 1952 lists 15 barbiturates Few physicians use more than three or four in their practice If the effects of these are well known from personal observation no others need be used unless more efficient ones become available It is to be remembered that barbiturates if long continued in use may lead to addiction they are habit-forming drugs This, however is hardly more than a theortical consideration for the average patient with an acute infectious disease which with modern chemotherapy rarely continues for more than three weeks and seldom that long

Barbital earlier in general use is now rarely prescribed for infectious diseases For a quick effect of relatively short duration and little after-effect next morning secobarbital sodium (Seconal Sodium) 0 1 to 0 2 gm pentobarbital sodium (Nembutal Sodium) 0 05 to 0 1 gm, or amobarbital (Amytal) 0 1 to 0 2 gm is suggested For a more prolonged effect phenobarbital 0 1 to 0 2 gm barbital sodium, 0 3 gm or butethal (Neonal) 0 05 to 0 1 gm may be used In general the larger doses recommended will prolong the action while with smaller doses the effect is less prolonged thus the physician can regulate by size of dosage the effect necessary for each patient

Chloral hydrate and paraldehyde are no longer used as frequently as sedative hypnotics in the treatment of infectious diseases barbiturates have for the most part replaced them Occasionally chloral hydrate may be desirable given in iced orange juice in doses of 0 3 to 1 0 gm, when needed larger doses of 2 gm may be used Paraldehyde is unpleasant to many owing to its persistingly disagreeable taste and odor When

and/or sweating there is a more than normal loss of fluid from the body resulting in varying degrees of dehydration—and this is very undesirable Consequently at least 2000 cc of fluid and often as much as 4000 to 5000 cc should be given The dryness of mouth, lips and skin and the amount of urine are simple indices of dehydration The urine output should be not less than 1500 cc preferably 2000 cc or more, each 24 hours Hematocrit readings form another index of possible dehydration but usually they are not necessary in the care of these patients The observant experienced physician can easily detect injurious dehydration and can also avoid an excess intake of fluid that might be too great a burden on the circulation

It is important that patients with infectious diseases in which there will probably be more than a week s duration of fever receive an adequate supply of sodium chloride with their diet Particularly if the diet is low in sodium chloride as is usually true when liquids and carbohydrates make up much of the ingested food or if the patient sweats has diarrhea or puts out a large amount of urine salt in 5 to 7 gm amount should be added to some part of the diet Such patients usually relish the added salt and if they are strong enough like to shake it on their food or at least see it shaken on If the diet includes butter it should be the salted variety

If dehydration is marked or if it is only moderate but the patient has difficulty in taking sufficient fluid by mouth normal saline solution with or without 5 or 10 per cent glucose should be given intravenously slowly in amounts of 500 to 1000 cc in each injection or continuously by the drop method the total amount in 24 hours to make up the patient s deficiency in fluid intake

Hydrotherapy

At one time an important part of the treatment of long continued fevers hydrotherapy now plays a less important role Cold or cool tub baths extensively used in the past in such diseases as typhoid fever are now given only in rare cases Some believe that by causing peripheral vascular constriction such tub baths decrease heat loss from the body They seem desirable however for patients with very high temperatures 105 F or over who do not respond to cool sponges an air current from an electric fan or other treatment Cool sponges or other forms of bed baths are very useful and should be given several times a

The position of the patient while eating or being fed should vary with his strength and the evidences of the fatigue being caused Change of position for feeding, if not too tiring or productive of considerable tachycardia, is desirable for many reasons one of which is improvement in morale

For a patient with nausea and a tendency to vomit, particular care in feeding is necessary to make certain that he receives sufficient calories of a diet adequate in protein carbohydrate fat, and vitamin content In the first place the patient s desire for a certain food or foods even though the request is unusual should be respected and the request should be met In the second place time for feedings should be selected so as to avoid a period of nausea Dry food well salted may be relished and retained by the patient who declines or even vomits liquids and soft solids For some patients gentle gastric lavage with subsequent tube feeding of varied liquids decreases nausea prevents vomiting and gives reasonable amounts of fluid containing desirable foods Finally if these measures fail parenteral fluid normal saline with 2½ to 5 per cent glucose, should be given by hypodermoclysis or intravenous drip technique in sufficient amount to prevent the development of any dehydration For some patients who are severely ill and are taking food and fluids poorly by mouth transfusions with blood or blood plasma are recommended When the need arises, and it rarely does to increase protein intake, a protein hydrolysate may be used to supplement other sources of protein

Always remember that nausea and vomiting may be due to the therapeutic agents being used If this is probable these agents should be discontinued and others substituted Too many pills may be in use A bed side chart of treatment always should be kept a busy attending physician may forget what treatments and when have been ordered

In a few patients with infectious disease especially those who vomit or sweat, a considerable loss of sodium chloride may have taken place if this occurs a corresponding amount of sodium chloride should be given Soft solid and fluid foods usually have inadequate salt content this deficiency should be made up by somewhere adding an amount to replace the deficit

Fluid Intake

The amount of fluid to be included in the diet is very important for patients with infectious diseases With the frequent high fever dyspnea

The following enemas are recommended 1 per cent sodium bicarbonate in tap water soap enema made by mixing 2 ounces of soap solution with 1 quart of tap water turpentine and egg white enema made by beating 2 to 4 cc of turpentine into the white of an egg and adding this to 1000 cc of water All enemas should be made with warm water and given before they cool

Any of the following mild cathartics may be tried given at bed time 15 to 30 cc of milk of magnesia 5 to 15 cc of aromatic fluid extract of cascara sagrada tablets containing 0 2 or 0 3 gm of extract of cascara sagrada Mineral oil is not advised

If more active catharsis is needed effervescent sodium phosphate U S P, 15 gm dissolved in a glass of water and followed immediately by another glass of water is excellent If vigorous catharsis is indicated magnesium sulfate 15 to 30 gm dissolved in a glass of water and followed immediately by a second glass of water is satisfactory but unpalatable In an occasional case oleum ricini (castor oil) proves helpful in a dose of 15 to 30 cc given at night in orange juice

Mineral oil is usually objectionable but may prove useful in cases with spastic rectal sphincter 30 to 60 cc may be injected into the rectum to serve as a lubricating medium

If diarrhea is present and is debilitating it should be treated It may be an expected result of the action of the causative agent of the infectious disease that the patient has — for example bacterial dysentery If so the treatment is mainly the special form of therapy advised for that particular disease If it is but an incident in the course of an infectious disease it may be related to the patient s diet and should be treated by simplification of diet or by the elimination of a food item possibly causing the diarrhea If diarrhea persists and is marked therapy to decrease intestinal peristalsis should be instituted as follows Camphorated tincture of opium [paregoric], 5 to 10 cc after each watery bowel movement is usually effective Some prefer to use powdered opium 60 mg every 4 hours

For milder diarrhea bismuth subcarbonate 1 gm every 2 to 3 hours or aluminum hydroxide gel containing 20 per cent kaolin (Kaomagma) 15 cc every 2 or 3 hours is suggested Obviously if the diarrhea is part of the patient's disease as in bacillary dysentery or Asiatic cholera, treatment of the disease as described under the specific headings on later pages is the most effective way of managing the diarrhea

If diarrhea is causing dehydration it is most important to correct it by giving adequate fluid usually intravenous normal saline solution with

day if they give comfort lessen nervous irritability, lower temperature, and slow the pulse

Mouth Care

Teeth and mouth should be cleansed by the patient if he is strong enough or by the nurse if the patient is unable to do so Any pleasant, mildly antiseptic mouthwash preferably the one the patient is accustomed to and likes should be used several times a day to rinse the mouth and teeth thoroughly For sicker patients and those with especially dirty and sore mouths irrigation with warm normal saline solution should be used For these cleansing is best done with pledgets of cotton moistened with a mildly antiseptic mouthwash The spaces between the teeth should be cleaned with dental floss three times a day if possible Following the use of dental floss the teeth should be brushed with a soft toothbrush using any dentifrice preferably the one ordinarily used by the patient

For very dry mouths slippery elm lozenges may be sucked or a mixture of glycerine and water to which have been added a few drops of lemon juice may be put into the mouth these as a rule overcome the unpleasant feeling of dryness

Bowel Care

The belief that catharsis is an important eliminant of noxious substances from patients with infectious diseases happily has passed These patients need their usual number of bowel movements — which means for some one a day for others one every second third or even fourth day So long as there is no abdominal distension or discomfort bowel movements are occurring often enough and there is no reason for increasing their frequency For many patients who do need induced bowel movements however a simple morning enema suffices for others a mild evening cathartic is better Many people are habituated to one or the other of these and this should guide the physician in his plan of bowel care during the course of an infectious disease He should be sure that the patient s complaints are not based merely on the belief which so many have that a daily bowel movement is essential to life and happiness

Bladder Care

In the majority of patients with acute infectious diseases there is no need of special attention to bladder function, which of course concerns chiefly an adequate amount of urine and necessary repetitions of bladder emptying. Adequate fluid intake will cause an adequate amount of urine. If the patient is somewhat stuporous the urinal should be adjusted every 3 or 4 hours and the patient urged to urinate. A patient who is unable to urinate while in bed should be allowed to stand up to urinate or to use a bedside commode. Stuporous patients, very ill patients or elderly men with some prostatic enlargement may be unable to urinate; they should be catheterized often enough to prevent bladder distension. Morphine is occasionally causative of spasm of the bladder sphincter; if this occurs atropine sulfate 0.3 mg. should be added to each dose of morphine or, better still, meperidine (Demerol) hydrochloride, 0.1 gm. or methadone hydrochloride 5 mg. can be substituted for the morphine.

Infection of the urinary tract, especially in patients requiring catheterization, may develop. If it does occur it can be recognized early by symptoms and by frequent urine examinations for all patients as often as once daily. When recognized it should be treated as described later under the headings Cystitis, Pyelitis and Pyelonephritis.

Skin Care

When there is fever, repeated cool sponging followed by rubbing with weak ethyl alcohol and the use of a dusting powder is comforting and helps to keep the patient's skin in good condition. All patients should have a cleansing bed bath daily unless some skin lesion contraindicates. Patients should be turned frequently from side to side to restrict pressure where bones are close to skin surfaces. Sweating patients should be dried frequently and powdered with a simple toilet powder containing starch. After urination and defecation adjacent skin areas should be inspected, cleansed and dried with scrupulous care. Bedsores should be prevented by these methods. If they begin they should be treated at once by careful cleansing and powdering and the area about them should be relieved of pressure by the use of inflated rubber rings or rings made of cleaned surgical gauze, which is better than previously unused gauze. If infection of the region about a bedsore

or without 5 or 10 per cent glucose

If abdominal distension occurs it should be treated promptly, since delay may increase greatly the difficulty of its effective management. Prompt inhalations of oxygen in high concentration by means of an appropriate mask may give quick relief. A rectal or high colonic tube may alleviate the discomfort if the distension is from gas in the rectum and lower colon; this is one of the simplest methods for relief. A mild enema of tap water, an enema containing magnesium sulfate, 30 gm., and glycerine, 60 cc. in 90 cc. of water, or a turpentine enema (Turpentine, 2 to 4 cc. and white of an egg in 1 quart of water) also may be effective, these are worthy of prompt trial. A soft small tube passed by mouth through the stomach into the intestine and a Wagensteen suction apparatus attached, as in cases of intestinal obstruction, will be effective when the small intestine is distended with gas. Some advise 15 to 30 cc. of castor oil by mouth in the early stages of abdominal distension, possibly repeating this for several days.

For some patients a change in diet with reduction in total amount of food and in carbohydrate content will decrease distension, although it is generally believed that defective peristalsis is more responsible for distension than are the amount and type of the food intake. Consequently, drugs to increase intestinal peristalsis and/or omission of those with the opposite effect often seem preferable in the treatment of distension. Heavy sedation, including opium derivatives, is often causative of distension and these drugs should be omitted or greatly reduced in amount if abdominal distension appears. This raises the question whether or not morphine in ordinary dosage can cause abdominal distension. Some believe that on the contrary a subcutaneous injection of 15 mg. of morphine will exert a tonic effect on intestinal musculature and will decrease distension. Drugs recommended to increase intestinal peristalsis in patients with abdominal distension may be used as follows: neostigmine (Prostigmine) methylsulphate or bromide, which may be given in a dose of 0.5 mg. (1.0 cc. of a 1:2000 solution) every half hour to one hour until the distention begins to subside or until minor toxic reactions such as salivation, nausea or flushing appear. If this treatment is successful and the distention is responding to the drug, the dose interval should be changed to 0.5 mg. every 2 to 3 hours. If neostigmine is ineffective, pituitary extract (Pitressin) 1.0 cc. of a 1:1000 solution may be tried. Care should be observed in its administration to cardiac or elderly persons in view of its coronary constricting effect.

Bladder Care

In the majority of patients with acute infectious diseases there is no need of special attention to bladder function which of course concerns chiefly an adequate amount of urine and necessary repetitions of bladder emptying Adequate fluid intake will cause an adequate amount of urine If the patient is somewhat stuporous the urinal should be adjusted every 3 or 4 hours and the patient urged to urinate A patient who is unable to urinate while in bed should be allowed to stand up to urinate or to use a bedside commode Stuporous patients very ill patients or elderly men with some prostatic enlargement may be unable to urinate they should be catheterized often enough to prevent bladder distension Morphine is occasionally causative of spasm of the bladder sphincter, if this occurs atropine sulfate 0 3 mg should be added to each dose of morphine or better still meperidine (Demerol) hydrochloride 0 1 gm , or methadone hydrochloride 5 mg can be substituted for the morphine

Infection of the urinary tract especially in patients requiring catheterization may develop If it does occur it can be recognized early by symptoms and by frequent urine examinations for all patients as often as once daily when recognized it should be treated as described later under the headings Cystitis Pyelitis and Pyelonephritis

Skin Care

When there is fever, repeated cool sponging followed by rubbing with weak ethyl alcohol and the use of a dusting powder is comforting and helps to keep the patient s skin in good condition All patients should have a cleansing bed bath daily unless some skin lesion contraindicates Patients should be turned frequently from side to side to restrict pressure where bones are close to skin surfaces Sweating patients should be dried frequently and powdered with a simple toilet powder containing starch After urination and defecation adjacent skin areas should be inspected cleansed and dried with scrupulous care Bedsores should be prevented by these methods If they begin they should be treated at once by careful cleansing and powdering and the area about them should be relieved of pressure by the use of inflated rubber rings or rings made of cleaned surgical gauze which is better than previously unused gauze If infection of the region about a bedsore

occurs, it should be treated promptly with appropriate antibiotics and antiseptics and should be incised and drained if pus develops With large intractable bedsores excision with plastic surgical repair is indicated In some patients scattered furuncles or boils may develop, these should have the usual surgical treatment and a sulfonamide, penicillin, streptomycin or other antibiotic as indicated by the type of infecting bacteria in relation to its sensitivity to these should be used With these agents available and used furuncles and boils rarely cause difficulty in skin care

CHAPTER II

SPECIFIC MEASURES

The most important agents at present in the treatment of infectious diseases are the specific antibacterial agents and antitoxins when such exist, they have replaced in large part other measures to control etiological agents Antitoxins are highly specific and their use in treatment will be discussed under the individual diseases in which they are used Antibacterial therapy consists of the use of specific immune sera sulfonamides penicillin bacitracin chloramphenicol (Chloromycetin) aureomycin and terramycin Under the headings of the individual diseases the appropriate antibacterial therapy if such exists will be stated A general discussion of the agents will be given here however — dosage techniques of administration and various general principles governing their use — to avoid later repetition

Antitoxins and Specific Immune Sera

Formerly, specific immune sera or antisera when such had been prepared were used often for then they constituted along with antitoxins almost the only available means for specific therapy Such were the antitoxins for diphtheria and tetanus and the antisera for the numerous types of pneumococci antimeningococcic serum, antistreptococcic serum and other less frequently used and less satisfactory antisera These except the antitoxins have been so satisfactorily supplanted today by other antibacterials such as sulfonamides penicillin streptomycin et cetera that they now are but rarely used and need little discussion

Since these agents are proteins they may cause a reaction when injected into man It is therefore essential to test the patient s sensitivity to the serum or antitoxin before administering the therapeutic dose This is done by making a 1 100 dilution of the serum and injecting 0 1 cc of it intracutaneously If no reaction occurs 0 1 cc of a 1 10 dilution may

then be tested intracutaneously or 1 drop may be instilled in the conjunctival sac of the eye If no reaction occurs within 30 minutes, it is safe to start the administration of a 1 10 dilution of the serum intravenously If this does not cause a reaction the therapeutic dose diluted in saline may be injected slowly The physician must be on the alert to detect the earliest signs of a reaction such as flushing, faintness itching, cough urticaria or dyspnea

If the reaction persists 0 [illegible] to 0 4 cc of a 1 1000 epinephrine (Adrenalin) hydrochloride solution should be given subcutaneously Mild reactions may be controlled by antihistaminic therapy Tripelennamine (Pyribenzamine) hydrochloride or diphenhydramine (Benadryl) hydrochloride 50 to 100 mg may be given orally and repeated at 15-minute intervals for 3 doses if the reaction persists

If instead of milder symptoms severe anaphylactic shock appears 0 5 cc of a 1 1000 epinephrine (Adrenalin) hydrochloride solution should be given subcutaneously and repeated in 15 minutes if necessary In extremely severe shock with cessation of breathing life has been saved by intravenous or, occasionally intracardiac injection of 0 5 cc of epinephrine solution along with artificial respiration and oxygen therapy

The immediate intramuscular injection of 80 mg of corticotropin or 300 mg of cortisone should be given in these severe reactions If the reaction persists [illegible]0 mg of corticotropin in 200 cc of normal saline given intravenously may be a life-saving measure

If such severe reaction does occur or if the patient has shown sensitivity to a test dose of the serum or antitoxin to be used a serum or antitoxin of other animal origin than the one that gave the reaction should be utilized if available or the patient should be desensitized by the injection of the offending serum or antitoxin, commencing with a subreactional intracutaneous dose and gradually increasing to larger amounts given subcutaneously as described under Bronchial Asthma

If after receiving serum or antitoxin patients develop urticaria or other allergic manifestations these often can be treated successfully by giving 50 mg doses of tripelennamine (Pyribenzamine) *hydrochloride* or other suitable antihistaminics by mouth 3 or 4 times a day

SULFONAMIDES

The sulfonamides are drugs having an antibacterial action on certain bacteria when given by mouth or intravenously in such plan of dosage

as will maintain a level of the drug in the blood stream high enough to inhibit growth of susceptible bacteria The needed blood level for this can be found by in vitro study of the growth of these bacteria in media containing varying concentrations of the sulfonamide A blood level of 10 to 15 mg per 100 cc is desirable in the treatment of those infectious diseases responsive to an easily absorbed sulfonamide Certain of the sulfonamides are poorly absorbed and so are to be used only in those diseases in which antibacterial effect is sought from their presence in the intestinal tract

Since the first of the sulfonamide group was prepared and used therapeutically numerous sulfonamides have been introduced the newer ones being less toxic and more effective than the older ones At present there are two groups used extensively enough to deserve description here of their therapeutic use One group is absorbed into the circulation after proper oral dosage in sufficient amount to maintain an effective antibacterial blood level The other group is poorly absorbed into the circulation but remains in the intestinal tract in sufficiently high concentration to inhibit the growth of bacteria present there Of the first group sulfacetamide sulfadiazine sulfadimetine sulfamerazine sulfamethazine sulfamylon sulfapyrazine and sulfisoxazole are recommended for therapeutic use of the second group succinylsulfathiazole (sulfasuxidine) phthalylsulfathiazole (sulfathalidine) and p nitrosulfathiazole have sufficient therapeutic effectiveness to be recommended in the treatment of certain diseases Organisms and infections susceptible to the sulfonamides are indicated in Table I On subsequent pages under the heading of each disease will be stated which sulfonamide if any is to be used in treatment Here the method of use dosage and toxic effects will be described so as to make repetition unnecessary when the treatment of each disease is being discussed

p Nitrosulfathiazole (*Nisulfazole*) This sulfonamide is helpful in the treatment of ulcerative colitis and proctitis It is relatively insoluble and consequently only small quantities are absorbed when it is given rectally as an instillation In the presence of severe ulceration larger amounts are found in the blood and care must be exercised to avoid overdosage Generally a dose of 10 cc of a 10 per cent suspension given after each bowel movement and at bedtime is satisfactory Occasionally doses of 30 to 60 cc are required for best results As improvement occurs the dose may be reduced to 10 to o cc once daily given at bedtime Treatment should be continued for 3 to 4 weeks after healing occurs

TABLE I

ORGANISMS AND INFECTIONS SUSCEPTIBLE TO THE SULFONAMIDES

- Actinomyces bovis
- Bacillary dysentery
- Bacillus (Escherichia) coli
- Bacillus Friedlander (Klebsiella pneumoniæ)
- Brucellosis (acute)
- Chancroid
- Clostridium septicum
- Clostridium welchii
- Gonococcal infections
- Hemophilus influenzæ
- Lymphogranuloma
- Meningococcal infections
- Pneumococcal infections
- Staphylococcal infections
- Streptococcal infections (B hemolytic Lancefield A B C, G)
- Streptococcus viridans (enteral)
- Urinary tract infections
  - Aerobacter aerogenes
  - Alcaligenes
  - Bacillus coli
  - Bacillus proteus
  - Bacillus pyocyaneus
  - Paracolon
  - Staphylococcus albus
  - Staphylococcus aureus
  - Streptococci

Phthalylsulfathiazole (Sulfathalidine) This sulfonamide is also poorly absorbed and should be given by mouth in a daily dose of 0 05 to 0 1 gm per kilogram of body weight daily The total daily dose is to be divided into 6 equal portions and given at 4 hour intervals A dose of 8 gm in 4 hours should not be exceeded When the drug is given before operation on the intestine an initial dose of 0 125 gm per kilogram of body weight is recommended followed each day by the same dose divided into 6 equal portions and given every 4 hours

Succinylsulfathiazole (Sulfasuxidine) also poorly absorbed remains in the intestinal tract in sufficient concentration to have an injurious effect on susceptible bacteria that may be present there It is to be administered orally The initial dose should be 0 25 gm per kilogram of body weight followed by a daily maintenance dose of 0 -5 gm per kilogram divided into 6 portions and given every 4 hours day and night, until the desired effect has been produced

Sulfabenzamine (Sulfamylon Marfanil) Sulfabenzamine is one of the newer sulfonamides and apparently has a different mechanism of action It is not inhibited by para aminobenzoic acid and therefore is active in the presence of pus and blood It is effective against pneumococci streptococci staphylococci and other sulfonamide susceptible organisms Anaerobic bacteria are also controlled The most effective use is by topical application as a 1 or 5 per cent solution Administered in this manner it is useful in the treatment of otitis externa chronic otitis media, sinusitis and infected wounds

Sulfacetamide (Sulamyd) Sulfacetamide has a range of usefulness similar to sulfadiazine It is given by mouth, preferably after meals in a dose of 1 0 gm 3 times a day for adults Children should receive 60 mg per kilogram of body weight daily the total dose divided and given by mouth after meals After 2 or 3 days with a daily dose in these recommended amounts, the dosage may be reduced to one half or one third and the patient maintained satisfactorily Generally the drug should be given for at least a week after the temperature has fallen to normal and all symptoms have disappeared Although sulfacetamide is claimed to have less toxicity, the same precautions as recommended for sulfadiazine should be observed, and if any untoward reactions appear, the drug should be discontinued at once

Sulfacetamide is effective in the treatment of urinary tract infections such as acute cystitis or pyelitis caused by E Coli or A Aerogenes organisms A 30 per cent solution of its sodium salt is useful in the treatment of trachoma and other eye infections caused by susceptible organisms

Sulfadiazine This sulfonamide is to be given by mouth in tablet form with an initial dose of 4 0 gm followed by a dose every 4 hours continued through the 24 hour period of 1 to 1 5 gm as needed to maintain the desired blood level of 10 to 15 mg per 100 cc of blood depending on the susceptibility of the infecting organism to sulfadiazine This dosage should be continued until the temperature approaches normal and then half this dosage given for several more days Some prefer to continue full dosage or to increase the interval between doses from 4 to 6 hours until the drug is stopped Minor toxic reactions such as nausea skin rash or slight fever should not cause cessation of the use of sulfadiazine, severe reactions, such as marked hematuria with oliguria or anuria hemolytic anemia, or agranulocytosis should cause immediate cessation and the use of another drug in most instances penicillin but in some bacterial infections streptomycin or another antibiotic should be started at once

A frequent toxic effect of sulfadiazine is hematuria This usually can be prevented by giving the patient sufficient fluid to produce a 24 hour urine output of 1500 cc or more Attention to this is particularly necessary in the patient who is sweating or in patients in the tropics Urine should be examined daily for the presence of red blood cells If such appear, fluid intake should be increased and the urine rendered all aline by the administration of sodium bicarbonate every 4 hours for all alinization of the urine usually 6 0 gm of sodium bicarbonate is needed as an initial dose followed by 2 5 to 5 gm every 4 hours It is essential to give

the amount needed to keep the urine alkaline in reaction rather than to follow a predetermined schedule of dosage of sodium bicarbonate If hematuria of considerable degree persists sulfadiazine should be stopped and penicillin or other chemotherapeutic agent should be given, whichever is the more effective against the infecting organism If urine flow greatly decreases or stops in spite of the alkalinization of the urine and the ureters and kidneys are blocked with crystals steps should be taken to carry out lavage of the hilum of each kidney through a ureteral catheter

For very sick patients for patients in coma and for patients infected with highly resistant bacteria sulfadiazine in the form of its sodium salt should be given intravenously until the patient improves or is able to swallow the tablets of sulfadiazine Return to mouth dosage should be made as speedily as the patient's condition will permit The sodium salt of sulfadiazine in a 5 per cent solution should be given in an initial dose of 5.0 gm intravenously followed by 2.0 gm every 8 to 12 hours so long as intravenous dosage seems needed As this solution is strongly alkaline great care should be used to prevent its escape into the tissues, since if this occurs it will be highly irritating and may cause necrosis with sloughs Venous thrombosis may follow this route of dosage

For children the initial oral dose of sulfadiazine should be 0.1 to 0.15 gm per kilogram of body weight followed by one fourth the initial dose every 6 hours until the temperature has been normal for several days

All dosage should be controlled by frequent determinations of the blood concentration of the drug whenever possible

Sulfadimetine (Elkosin) One of the most recently introduced sulfonamides sulfadimetine shows promise Preliminary use indicates that it is acetylated only to a slight extent is readily absorbed and excreted So far toxic reactions have been infrequent The wide antibacterial spectrum covered by this drug its solubility and its wide distribution in tissue make it useful in the treatment of many infections most especially those of the genito urinary tract It is active against those organisms susceptible to the sulfonamides

A dose of 2.0 to 4.0 gm initially, depending on the severity of the infection followed by 1.0 gm every 4 hours is recommended for systemic infections Localized genito urinary infections usually respond to a dose of 1.0 gm initially followed by 1.0 gm every 8 hours The drug should be continued until all signs and symptoms have been

relieved for at least 3 to 6 days Children should receive a daily dose of 0 1 gm per kilogram of body weight

Hematuria is rare with this sulfonamide but the possibility of sensitivity reactions is present and therefore the same precautions as recommended for sulfadiazine must be observed

Sulfamerazine This sulfonamide is absorbed more rapidly and excreted more slowly so that smaller doses and longer intervals between *doses than with sulfadiazine are needed to maintain adequate blood levels*

For sulfamerazine the usual initial dose should be 3 0 to 4 0 gm followed by 1 0 gm at 8 hour intervals For intravenous use the initial dose of the sodium salt should be 5 0 gm followed by 2 0 gm every 12 hours For children the initial dose of sulfamerazine should be 0 1 gm per kilogram of body weight followed every 12 hours by one half the initial dose

Except for the difference of dosage all that has been written about sulfadiazine applies to sulfamerazine

Sulfamethazine Another pyrimidyl derivative that has action similar to that of sulfadiazine is sulfamethazine It is absorbed in a manner similar to that of sulfadiazine and is excreted somewhat more rapidly than is sulfamerazine Because its renal clearance resembles that of *sulfamerazine it also tends to accumulate in the blood if renal function* is lowered It is acetylated more rapidly than sulfadiazine or sulfa merazine and is bound to protein to a greater degree

A dose of 0 1 gm per kilogram of body weight is recommended in severe infections but the total initial dose in adults should not exceed 5 0 gm A maintenance dose of 1 0 gm given at 6 hour intervals is usually satisfactory Children should receive one fourth of the initial dose at 6 hour intervals The same precautions as recommended for sulfadiazine must be observed

Sulfapyrazine This sulfonamide resembles sulfadiazine in its actions and toxicity It is however absorbed and excreted rather slowly Acetylation is much reduced A cerebrospinal fluid level of one half to two thirds the blood level can be obtained by intravenous administra tion of the sodium salt

For adults an oral dose of 2 0 to 4 0 gm initially followed by 1 0 gm doses at 4- to 6 hour intervals until the temperature has been normal for 3 days is recommended Infants under 6 months usually can be given 0 5 gm initially followed by 0 25 gm every 6 hours Older children under 3 years of age may be given 1 0 gm initially followed by 0 5 gm every 6 hours Children over 3 years of age may be given an initial dose

of 2 0 gms followed by 1 0 gm every 6 hours

Sulfisoxazole (Gantrisin) Sulfisoxazole a recently introduced sulfonamide, shows much promise of being a useful addition to the antibacterial agents It exhibits low toxicity, and renal complications are infrequent It is to be given by mouth in an initial dose of 4 to 6 gm (the greater dose recommended for larger and heavier patients) and followed by 1 to 2 gm at 4 hour intervals until the temperature has been normal for at least 3 days or until urine cultures become and remain sterile If intravenous therapy is indicated 4 0 gm (one 10 cc ampule) of the diethanolamine salt is given by slow intravenous injection and repeated at 8- to 12-hour intervals until the drug can be taken by mouth or the infection is controlled For children an initial dose of 0 1 gm per kilogram of body weight followed by 0 02 gm per kilogram every 4 hours is recommended

Sulfisoxazole is effective against a wide variety of organisms and is very useful in the treatment of infections of the genito urinary tract Fortunately it is effective against some strains of *Bacillus pyocyanus* and *B proteus* and consequently is most useful in these cases

The usual precautions taken with other sulfonamides are necessary In general the incidence of complications appears to be less than with the other drugs in the series Usually it is not necessary to alkalinize the urine with sodium bicarbonate since renal complications are not common If such complications do appear, the treatment recommended for sulfadiazine should be used

Antibiotics

Penicillin Penicillin is therapeutically superior to the sulfonamides for organisms and diseases in which both are effective, it is also effective in some conditions that do not respond to sulfonamide therapy Its very low toxicity gives it a great advantage over other antibacterial agents Except for an occasional urticarial reaction toxicity even when penicillin is given in very large doses is almost lacking There is reason to believe however that the incidence of toxic reactions is increasing as the drug continues in use The most common reaction to penicillin is sensitivity, with resultant urticaria pruritus and peeling of the skin Occasionally severe anaphylactic reactions occur Local tissue reactions such as glossitis from the use of troches or dermatitis from the application of penicillin ointment, occur in a few patients Care must be exercised in

the presence of any of these manifestations and the drug stopped or treatment shifted from the usual penicillin G to penicillin O or Ephenamine penicillin G (Compenamine) The ointment has such a high index of local sensitivity reactions that its use is not recommended Occasionally sensitivity to the procaine moiety occurs requiring a shift to ordinary penicillin or to another suitable antibiotic

Penicillin s chief disadvantage lies in its relatively lower efficiency by oral dosage This makes the parenteral route preferable for its use Table II shows the organisms that are susceptible to penicillin

TABLE II

Organisms Susceptible to Penicillin

Bacillus anthracis
Bacillus subtilis
Clostridia
Corynebacterium diphtheriae
Gonococcu
Hemophilic organisms
Leptospira icterohaemorrhagiae
Listerella monocytogenes
Meningococcus
Micrococcus tetragenus
Pneumococcus
Spirillum cholerae (Vibrio comma)
Spirillum minus
Spirillum novyi
Spirillum rubrum
Staphylococcus albus
Staphylococcus aureus
Streptobacillus moniliformis
Streptococcus hemolyticus
Streptococcus viridans
Treponema pallidum
Treponema pertenue
Vincent s spirillum

To use penicillin most effectively the susceptibility of the infecting organism should be tested in vitro when that is possible and the dosage to be used should be based on this test This is of very great importance in the treatment of subacute bacterial endocarditis Some organisms require much higher blood levels than others to overcome infection If such testing is not possible the dosage representing the usually effective number of units as indicated in the following paragraphs should be used and if these doses seem clinically unsatisfactory they should be increased It is assumed in this advice that the infecting organism is one known to be susceptible to penicillin but is one requiring more than the average dose because its level of resistance is higher than is usual It does not follow that penicillin should be used blindly in increasing dosage determination of the degree of susceptibility of the infecting organism is a prerequisite to the satisfactory usage of penicillin whenever it is apparent that the average recommended dosage is not being effective

Although penicillin can be given most effectively by the parenteral

route it is also effective when given by mouth Absorption of penicillin from the gastro-intestinal tract is slow and incomplete, so that to obtain good results oral dosage needs to be at least 4 to 5 times greater than by other routes There are various procedures that can be followed to increase gastro-intestinal absorption but the most important factor is to give adequate dosage while the stomach is empty A dose range, by mouth of from 100 000 units 2 times a day to 400,000 units 3 times a day, depending on the sensitivity of the organism, is recommended Since penicillin is now available in large quantities at economical prices oral use should be employed more frequently than it has been in the past There is less incidence of reactions when the drug is given by mouth

Penicillin should be dissolved in physiological saline solution for intravenous or intramuscular injection The continuous intravenous or 3-hourly intermittent intramuscular method is recommended for acutely ill patients and for patients infected with highly resistant organisms The use of crystalline procaine penicillin either in aqueous solution or suspended in sesame oil makes it possible to give intramuscular injections at 12 to 24 hour intervals and still maintain therapeutic levels These forms of dosage are being used with increasing frequency, especially in non hospitalized patients

Penicillin for intravenous or intramuscular injection should be freshly dissolved in normal saline solution so that each cc contains from 10,000 to 50,000 units For continuous injection the rate should be from 5,000 to 50 000 units per hour Intermittent injections should be repeated at intervals of 2 to 3 hours day and night Total dosage should range from 300 000 to 1,000 000 or more units per 24 hours Procaine penicillin should have a concentration of 300 000 units per cc, and such amounts should be given at 12- to 24 hour intervals This form of penicillin administration should be limited according to some to milder infections or substituted in cases where the acute phase is over since absorption is so slow that sufficiently high levels of the drug are not obtained quickly enough to combat acute infections Many now prefer this form of usage, however, except in a rare case of fulminating severity Newer preparations containing 100 000 units of soluble penicillin suspended with 300 000 units of procaine penicillin overcome much of this objection

When given intravenously or intramuscularly penicillin reaches the cerebral tissues only in low concentration Consequently, when it is used in the treatment of patients with meningitis caused by penicillin susceptible organisms it may need to be given intrathecally in addition to

the other routes For this method a concentration of 1000 units per cc should be used Before administration 15 to 20 cc of spinal fluid should be withdrawn this should then be replaced by a corresponding amount of the penicillin solution giving a total intrathecal dose of 15,000 to 20 000 units of penicillin Some observers believe that the intrathecal route is seldom necessary

Penicillin can be used also for injection into infected cavities such as empyema cavities, prior drainage of the cavity is usually necessary however When the patient is acutely ill penicillin may be injected into these cavities in dosage of 100 000 to 500,000 units daily in addition to giving it intravenously or intramuscularly when the infection is chronic the intravenous administration may be omitted

Penicillin may be given also as an aerosol by nebulizing in a suitable apparatus a solution containing 25 000 to 50 000 units This method is not very satisfactory and is being used much less than it formerly was

It is to be remembered that especially with inadequate dosage other wise susceptible organisms may become penicillin resistant If relapses are to be avoided, treatment must be continued until the patient has been afebrile for at least 3 days

Under the discussion of individual diseases in later pages the par ticular methods form and the size of doses that seem most desirable for usage will be indicated

Streptomycin and Dihydrostreptomycin are indicated for the infec tions listed in Table III For some infections they are still the only ef fective antibiotics They are of considerable value in some forms of tuberculosis

Streptomycin gives many more toxic reactions than does penicillin A histamine like reaction with a fall of blood pressure and syncope may

TABLE III

ORGANISMS SENSITIVE TO STREPTOMYCIN

Aerobacter aerogenes	Mycobacterium tuberculosis
Brucella	Pasteurella leptiseptica
Corynebacterium diphtheriae	Pasteurella pestis
Eberthella typhi (some strains)	Pasteurella tularensis
Escherichia coli	Proteus vulgaris
Escherichia communior	Pseudomonas aeruginosa
Hemophilus influenzae	Salmonella enteritidis
Hemophilus pertussis	Shigella paradysenteriae
Klebsiella ozaenae	Staphylococcus aureus (some strains)
Klebsiella pneumonia (Friedlander s bacillus)	

follow its use A neurotoxic action on the eighth nerve occurs in about 10 per cent of patients receiving streptomycin, this reaction is characterized by vertigo tinnitus and decreased auditory acuity, recovery is slow and deafness may persist Skin rashes, malaise, muscular aches, and drug fever also may accompany its use

Streptomycin needs to be given parenterally For intravenous use 1 to 2 gm of streptomycin should be dissolved in 1000 cc of normal saline solution and administered by the intravenous drip method at a rate of .4 drops per minute so that the patient receives 1 to 4 gm of streptomycin every 24 hours for 48 to 7 hours depending on the severity of the infection and the sensitivity of the invading organism to the antibiotic Streptomycin may also be given intermittently every 3 hours by vein or intramuscularly in divided doses to a total per 24 hours of 2 to 4 gm dissolved in normal saline solution in a strength of 100 to .00 mg of streptomycin per cc

For intrathecal injection 10 to .0 mg per cc in normal saline solution should be used, giving 10 to 15 cc of this every 3 hours For injection into infected cavities 1 to . gm of streptomycin dissolved in normal saline solution should be used For topical applications, solutions containing .5 to 50 mg per cc may be used Care must be exercised in using streptomycin topically because of the tendency for severe local sensitivity to develop

In the use of streptomycin it is very important to give sufficiently large doses to inhibit or kill the infecting organisms quickly, since the development of fastness to streptomycin occurs easily and may take place very rapidly Inadequate dosage predisposes to the development of strains of organisms resistant to streptomycin For best results the in vitro resistance of the organisms to streptomycin should be tested as a measure for the optimum dosage The frequent and rapid development of fastness to streptomycin is a potential cause of ineffectiveness in streptomycin therapy

Dihydrostreptomycin can be used in place of streptomycin although it is no more effective It is given in the same dose and manner as streptomycin Occasionally it can be used in place of streptomycin when sensitivity reactions to the latter have developed

Aureomycin Hydrochloride Aureomycin the golden yellow antibiotic produced by the soil organism *Streptomyces aureofaciens*, is chemotherapeutically effective against a wide spectrum of organisms and a limited group of viruses (see Table IV)

TABLE IV

ORGANISMS SENSITIVE TO AUREOMYCIN

Aerobacter aerogenes	Rickettsial infections
African tick bite fever	Salmonella infections — some varieties but not typhoid fever
Amebiasis	Shigella
Anthrax	Staphylococcal infections
Bacteroides	Streptococcal infections
Boutonneuse fever	Treponema pallidum
Brucella	Tularemia
Clostridium welchii	Viral infections
Escherichia coli	Infectious mononucleosis — possibly of value
Gonococcus	Lymphocytic choriomeningitis
Granuloma inguinale	Lymphogranuloma venereum
Hemophilus infections	Ornithosis
Moraxella lacunata (Diplobacillus Morax Axenfeld)	Primary atypical pneumonia
Pleuropneumoniae	Psittacosis
Pneumococcus infections	
Proteus vulgaris	

Miscellaneous infections in which aureomycin may be of limited value

Borrelia	Herpes zoster
Dermatitis herpetiformis	Leptospira icterohaemorrhagiae
Eczema vaccinata	Molluscum contagiosum
Fusospirochetosis	Spirillum minus — rat bite fever
Herpes simplex	Trichomonas vaginalis

When given by mouth aureomycin is rapidly absorbed and widely distributed in the body The toxicity is low and in those patients with the more severe reactions consists chiefly of nausea vomiting and diarrhea On rare occasions a mild glossitis similar to that seen with penicillin is observed Aureomycin should be given by mouth since it produces considerable tissue irritation when given intramuscularly and phlebitis not infrequently follows intravenous injections If intravenous injections are necessary the drug should be well diluted in 500 to 1000 cc of 5 per cent glucose or normal saline and given slowly All of the drug must be thoroughly washed into the vein before removal of the needle The insertion of a small venous catheter into the vein occasionally is helpful in preserving the vein in acute cases where repeated intravenous therapy is necessary

Effective dosage consists of 20 mg per kilogram of body weight given in 4 equal doses over a 24 hour period For the average patient this consists of 0 25 gm every 6 hours Treatment in full dosage should be

follow its use A neurotoxic action on the eighth nerve occurs in about 10 per cent of patients receiving streptomycin, this reaction is characterized by vertigo tinnitus and decreased auditory acuity, recovery is slow and deafness may persist Skin rashes malaise, muscular aches, and drug fever also may accompany its use

Streptomycin needs to be given parenterally For intravenous use 1 to 2 gm of streptomycin should be dissolved in 1000 cc of normal saline solution and administered by the intravenous drip method at a rate of 24 drops per minute so that the patient receives 1 to 4 gm of streptomycin every 24 hours for 48 to 72 hours depending on the severity of the infection and the sensitivity of the invading organism to the antibiotic Streptomycin may also be given intermittently every 3 hours by vein or intramuscularly in divided doses to a total per 24 hours of 2 to 4 gm dissolved in normal saline solution in a strength of 100 to 200 mg of streptomycin per cc

For intrathecal injection 10 to 20 mg per cc in normal saline solution should be used giving 10 to 15 cc of this every 3 hours For injection into infected cavities 1 to 2 gm of streptomycin dissolved in normal saline solution should be used For topical applications solutions containing 25 to 50 mg per cc may be used Care must be exercised in using streptomycin topically because of the tendency for severe local sensitivity to develop

In the use of streptomycin it is very important to give sufficiently large doses to inhibit or kill the infecting organisms quickly since the development of fastness to streptomycin occurs easily and may take place very rapidly Inadequate dosage predisposes to the development of strains of organisms resistant to streptomycin For best results the in vitro resistance of the organisms to streptomycin should be tested as a measure for the optimum dosage The frequent and rapid development of fastness to streptomycin is a potential cause of ineffectiveness in streptomycin therapy

Dihydrostreptomycin can be used in place of streptomycin although it is no more effective It is given in the same dose and manner as streptomycin Occasionally it can be used in place of streptomycin when sensitivity reactions to the latter have developed

Aureomycin Hydrochloride Aureomycin the golden-yellow antibiotic produced by the soil organism *Streptomyces aureofaciens*, is chemotherapeutically effective against a wide spectrum of organisms and a limited group of viruses (see Table IV)

phenicol. Others will undoubtedly be added to this list as experience with the drug increases.

Chloramphenicol because of its wide spectrum markedly alters the bacterial flora of the upper respiratory tract and produces a nearly sterile nasopharynx. This property makes it a most useful prophylactic agent for the suppression of those infections likely to cause rheumatic fever, glomerular nephritis, bacterial endocarditis and so forth.

When given by mouth the drug is rapidly absorbed and widely distributed in the tissues. There has been very little toxic effect noted. Nausea, vomiting and diarrhea, however, are commonly observed. In general these symptoms are somewhat less than that observed with aureomycin. Chloramphenicol is much less toxic than streptomycin.

Chloramphenicol is best given by mouth in an initial dose of 60 mg per kilogram of body weight divided in 3 doses and given at hourly intervals; this should be followed by a 2-4 hour dose of 30 to 100 mg per

TABLE X

ORGANISMS SENSITIVE TO CHLORAMPHENICOL

- Aerobacter aerogenes
- Amebiasis
- Brucella
- Corynebacterium
- Escherichia coli
- Gonococcus
- Hemophilus pertussis
- Klebsiella
- Meningococcus
- Pneumonococcus
- Proteus vulgaris
- Pseudomonas aeruginosa
- Rickettsial infections
- Salmonella
- Shigella
- Staphylococcus infections
- Streptococcus infections
- Tularemia
- Virus infections
  - Lymphogranuloma venereum
  - Primary atypical pneumonia
  - Psittacosis

kilogram of body weight, depending on the severity of the infection, divided and given at 4- to 6-hour intervals. A dose of 0.5 gm, increased in more serious cases to 1.0 gm, 4 times a day also is usually satisfactory. Treatment should be continued until the temperature has been normal for at least 2 days. In treating typhoid fever and urinary tract infections the drug should be continued for at least a week after the temperature is normal and the urine has cleared, in a dose of 250 mg 4 times a day, if relapse is to be avoided.

Diarrhea, rectal irritation and rarely glossitis may follow the use of chloramphenicol, but these mild complications clear rapidly when the drug is discontinued. When chloramphenicol is continued over a

continued for 2 days after the temperature has returned to normal Infections not responding promptly should receive 0 25 gm every 3 hours

Intravenously a dose of 250 to 500 mg twice a day is recommended The solution should be freshly prepared by adding the desired amount to 500 to 1000 cc of normal saline or 5 per cent glucose solution, and it should be injected slowly into the vein

A more concentrated preparation consisting of 100 mg in 10 cc of glycine diluent may be used If this preparation is used, the needle should be a -- gauge, and the injection made very slowly, no more than 10 cc being given over a 5-minute period

For topical therapy a 3 per cent ointment is available for dermatological uses, and there is a 0 1 per cent ointment for ophthalmological needs When the drug is desired in ocular infections 1 or . drops of a 0 5 per cent solution of aureomycin borate applied to the eyes every 1 or 2 hours is excellent in severe infections

Some of the nausea and gastro intestinal distress can be relieved by having the patient eat a small amount of food such as a glass of milk or a few crackers, before taking the drug Diarrhea, if it becomes a problem is readily controlled by aluminum hydroxide gel, 15 cc every 3 or 4 hours or camphorated tincture of opium [Paregoric], 4 cc every 3 or 4 hours Aluminum hydroxide absorbs some of the aureomycin and some of the dosage is lost by bowel, consequently it should not be given if there is severe infection or if the patient is not responding favorably

If aureomycin is administered for a week or more deficiencies of vitamins of the B complex and of vitamin K may appear Diarrhea may contribute to these deficiencies They should be prevented by supplemental vitamin therapy consisting of at least 3 times the normal daily requirements

Chloramphenicol (Chloromycetin), isolated from *Streptomyces venezuelae*, is another effective antibiotic against a wide spectrum of sensitive organisms The chemical structure is known and the drug has been synthesized Although the action of chloramphenicol rather closely resembles that of aureomycin there is an important difference between the two as regards action against the Salmonella organisms Chloramphenicol is highly effective against these organisms It is apparently the only antibiotic proved to be highly effective against typhoid fever Listed in Table V are organisms known to be sensitive to chloram-

be given For infants and young children under 20 kilograms in weight a dose of 150 mg per kilogram of body weight per day divided into 4 equal doses is satisfactory When the drug cannot be given by mouth it may be given intravenously in a dose of 0 5 to 1 0 gm a day The desired dose should be diluted in at least 100 cc of normal saline solution or 5 per cent dextrose solution before administration The infusion should not contain more than 5 mg of terramycin per cc and the rate of injection should not exceed 100 cc in 5 minutes The drug must not be given subcutaneously or intramuscularly and care should be taken to see that the needle is well inserted into the vein before the injection is begun

When terramycin is continued over a week supplementary vitamins as recommended for use with aureomycin therapy should be given

Bacitracin This antibiotic isolated from the Tracy strain of *Bacillus subtilis*, has now been purified and found to be effective against a large variety of organisms It has been used chiefly as a topical application for wounds and skin infections Used in this manner it has proved very effective Pyogenic skin infections are cleared rapidly and wound infections including the difficult to manage bacterial synergistic gangrene lesions respond favorably It has also been shown to be effective when given by mouth in the treatment of amebiasis Although the purified derivative is much less toxic there is still the possibility of renal irritation when large doses are given parenterally The drug is not stable Solutions must be kept under refrigeration and discarded after 2 or 3 weeks When bacitracin is used as a topical agent or for limited local infiltration a solution containing 500 units per cc in sterile isotonic saline solution is employed For local infiltration the solution should contain 1 per cent procaine Ointments containing 500 units per gram are effective For the treatment of amebiasis bacitracin may be given by mouth in a dose of 20 000 to 60 000 units every 6 hours

Patients receiving bacitracin should be watched closely since renal damage may occur especially when large doses are given Bacitracin has a low allergic index and very little skin irritation has been produced by its local use

Neomycin, a recently developed antibiotic obtained from streptomyces culture No 3535 shows promise of being effective against a wide variety of organisms Clinical experience is still too limited to assign this agent a definite role in therapy It is heat stable and exhibits a bactericidal action in addition to its bacteriostatic effect

Combined Antibacterial Therapy Certain infections respond better

week, supplemental vitamin therapy as recommended for use with aureomycin therapy is indicated

Recently a number of serious cases of aplastic anemia with fatalities have been reported These have followed and apparently been caused by, the use of chloramphenicol The total number of cases is not large when compared with the total number of patients who have received the drug They indicate however, that it should not be used indiscriminately and probably should be reserved for patients with typhoid fever or infections that do not respond to other less toxic antibiotics Certainly great care must be exercised in its use and frequent evaluation of the patient s condition should be made during treatment Intermittent therapy should be avoided and the drug should be discontinued as soon as possible

Terramycin Another effective broad spectrum antibiotic is crystalline terramycin hydrochloride produced from *Streptomyces rimosus* It is a highly stable readily absorbed well-tolerated agent which may be given by mouth, rectum, or intravenously A few patients develop looseness of stools and mild nausea and occasionally vomiting has been noted Glossitis and proctitis as seen after the use of other antibiotics also may occur Table VI is a list of the organisms that are sensitive to terramycin as in the case of other antibiotics additional organisms undoubtedly will be placed on this list as experience increases

TABLE VI

ORGANISMS SENSITIVE TO TERRAMYCIN

Aerobacter aerogenes	Meningococcus
Amebiasis	Rickettsial infections
Anthrax	Salmonella infections
Bacteroides	Spirochetal infections
Brucella infections	Staphylococcus infections
Escherichia coli	Streptococcus infections
Gonococcus	Tularemia
Granuloma inguinale	Virus infections
Hemophilus infections	Lymphogranuloma venereum
Klebsiella pneumoniae	Primary atypical pneumonia

Terramycin may be given by mouth or intravenously The oral dose in adults is 2 to 3 gm daily divided into 4 equal doses In severe infections an initial dose of 1 gm and a total daily dose of 4 to 6 gm should

long acting preparation absorbed on aluminum phosphate gelatin or other binding agents, it may be given once in 12 24 or 48 hours depending on the daily dosage required In general when the long acting preparation is used, a daily dose of 70 mg or more requires injections at 12 hour intervals while a dose of 50 mg requires an injection once in 24 hours Daily doses smaller than 30 mg may be given once in 48 hours depending on the patient s response When a rapid intense effect is desired corticotropin may be given intravenously as a continuous infusion over a period of 8 hours in a dose of o mg dissolved in 500 cc of saline

Cortisone is usually given intramuscularly as a saline suspension in a dose of 50 to 100 mg or more a day It also may be given by mouth in an oral dose of 100 mg or more a day There is some cumulative effect and action may persist for as long as 3 days after therapy is discontinued

The uses of these agents are manifold and new uses are being discovered continually In general their chief value lies in the management of acute diseases of short duration which respond readily to their action patients with chronic conditions requiring long term treatment or large dosage are likely to develop undesirable reactions which seriously curtail their usefulness In the following table are listed the diseases usually showing some response to these agents

TABLE VIII

A DISEASES IN WHICH THE USE OF HORMONES IS ADVISABLE

Disease	*Hormone*	*Results*
Acute drug sensitivity	corticotropin or cortisone	Good to excellent
Addison s disease	cortisone	Excellent but supplementary therapy with desoxycorticosterone or sodium chloride is required
Adrenal androgenic hyperplasia	cortisone	Helpful
Adrenal cortical insufficiency	cortisone	Excellent
Anorexia nervosa	corticotropin	Fair
Contact dermatitis	corticotropin or cortisone	Good
Disseminated lupus erythematosis	corticotropin or cortisone	Fair hormones tend to hold the disease in abeyance

when combinations of antibacterial agents are used Unfortunately in some instances there is apparently a decrease in effectiveness when certain of these agents are used together Table VII lists those diseases where combined therapy is useful

There is evidence indicating that penicillin may be less effective when used in combination with aureomycin chloramphenicol, or terramycin Any organism not responding promptly to a combination of these agents may become resistant to penicillin Apparently penicillin and streptomycin are not antagonistic and usually make a very effective combination

TABLE VII

Bacterial Meningitis	Penicillin and sulfonamides
Mixed bacterial infections	Penicillin streptomycin and sulfonamides
Brucellosis	Streptomycin and aureomycin
Tuberculosis	Streptomycin and para aminosalicylic acid

Corticotropin (ACTH) and Cortisone

These preparations have important uses in treatment They are not specifically curative of any disease but they bring about speedily marked changes in body economy changes that may be either definitely ameliorative of serious symptoms or injurious to the patient receiving them Injurious effects are often rather slow to appear and frequently they persist sometimes long after the use of corticotropin or cortisone has ended These preparations must be given in the proper dosage to get the maximum of good effects and the minimum of injurious ones Frequent observation of the patient so as to recognize any incipient harmful effects is necessary When they appear they must be balanced against potential good effects in determining whether to continue usage of corticotropin or cortisone and in what dosage and for how long Since corticotropin can produce its action only through stimulation of the adrenal cortex it will be ineffective unless there is adequate adrenal cortical tissue to secrete the hormones that produce the desired effect It is therefore necessary to use cortisone in patients with adrenal cortical insufficiency

Corticotropin is a sterile powder which is dissolved in saline and usually given intramuscularly in a dose varying according to the patients needs of from 5 to 25 mg every 6 hours or as a slowly absorbed

Disease	*Hormone*	*Results*
Burns	corticotropin or cortisone	Helpful
Dermatomyositis	corticotropin or cortisone	Fair
Erythema nodosum	corticotropin or cortisone	Fair
Gout, acute	corticotropin or cortisone	Good — but disease tends to relapse unless colchicine is given most useful in cases refractory to colchicine
Multiple myeloma	corticotropin or cortisone	Fair — especially in blast type
Pemphigus	corticotropin or cortisone	Temporary help
Psoriasis	corticotropin or cortisone	Clears — but recurrence is the rule best results with discoid type exfoliative type tends toward exacerbations when hormone is withdrawn
Pulmonary beryllosis	corticotropin or cortisone	Temporary help
Regional enteritis	corticotropin or cortisone	Temporary help
Rheumatoid arthritis	corticotropin or cortisone	Excellent response but recurrence usually follows
Sarcoidosis	corticotropin or cortisone	Much improvement
Ulcerative colitis	corticotropin or cortisone	Fair response
Urticaria	corticotropin or cortisone	Excellent
Vasomotor rhinitis	corticotropin or cortisone	Excellent

C. Diseases in Which the Hormones are of Limited Value

Disease	*Hormone*	*Results*
Atopic dermatitis, chronic	corticotropin or cortisone	Permanent remissions are rare
Cancer	corticotropin or cortisone	Usually poor response
Leukemia and lymphosarcoma	corticotropin or cortisone	Most useful when combined with antifolic acid derivatives
Nephrotic syndrome	corticotropin or cortisone	Useful in producing diuresis
Scleroderma	corticotropin or cortisone	Most useful in early cases but therapy must be continuous

Disease	Hormone	Results
Exfoliative dermatitis	corticotropin or cortisone	Helpful
Hemolytic jaundice	corticotropin	Excellent in managing acute attacks
Hypoglycemia idiopathic	corticotropin	Excellent
Hypopituitarism functional or organic	corticotropin or cortisone	Excellent
Inflammatory or allergic diseases of the eye	corticotropin or cortisone	Good to excellent
Acute choroiditis Acute iridocyclitis Acute iritis Acute keratitis Acute uveitis Sympathetic ophthalmia Vernal conjunctivitis	corticotropin 25 mg every 6 hours for 1 week or cortisone intramuscularly 100 mg every 8 hours for 24 hours then 100 mg every 12 hours for 1 day followed by 100 mg daily Topical application of a suspension of cortisone 1 4 or 1 8 in saline 1 drop every hour is also effective Sub conjunctival administration of 0.05 cc of cortisone in suspension containing 1 25 mg daily for 3 or 4 days may also be given	
Loeffler's syndrome	corticotropin	Excellent
Periarteritis nodosa	corticotropin or cortisone	Temporary value inhibits acute process
Rheumatic fever acute	corticotropin or cortisone	Useful in arresting the process
Serum sickness	corticotropin or cortisone	Good
Toxic agents Black widow poison Snakebite	corticotropin	Excellent

B Diseases in Which the Hormones are Useful

Disease	Hormone	Results
Acute dermatomyositis	corticotropin or cortisone	Fair
Bronchial asthma	corticotropin or cortisone	Fair to good in acute in tractable cases—but disease tends to be worse when hormone is discontinued

provement in the cardiac status The loss of calcium resulting from the use of these agents makes it inadvisable to use them in the presence of osteoporosis and osteomalacia When their use is necessary in these cases the diet should contain supplemental calcium

Allergy to corticotropin may develop but it can be relieved in most cases by changing from corticotropin of one animal species to that of another or by shifting to cortisone Occasionally a patient becomes allergic to extracts of the pituitary per se These patients apparently are sensitive to corticotropin from all sources and in these cases cortisone must be used

BIBLIOGRAPHY

Chemotherapy

1 KEEFER C S and ANDERSON D G *Penicillin in the Treatment of Infections* Oxford University Press 1949

2 KING E Q LEWIS C N WELCH H CLARK E A Jr JOHNSON J B LYONS J B SCOTT R B and CORNELY P B Terramycin Hydrochloride *Jour Amer Med Assoc* 1950 cxliii p 1

3 LONG P H Clinical Use of Antibiotics *Med Clin No Amer* March 1950 p 307

4 ROMANSKY M J FUSILLO M H CALDWELL E L and ROBIN E D The Synergistic Action and Potential Applications of Antibiotic Combinations *Med Clin No Amer* March 1951 p 535

5 SMADEL J E Clinical Use of Chloramphenicol *Jour Amer Med Assoc* 1950 cxlii p 315

6 SPICER S Bacteriologic Studies of Newer Antibiotics Effect of Combined Drugs on Micro Organisms *J Lab and Clin Med* 1950 xxxvi p 183

7 FORSHAM P H Present Status of ACTH and Cortison in Therapy *Med Clin No Amer*, September 1951 p 1 29

D Disease In Which The Hormones May Be Harmful

- Acne
- Congestive heart failure (except certain cases of failure produced by acute rheumatic fever)
- Cushing s syndrome
- Diabetes mellitus
- Hirsutism
- Hypertension
- Osteoporosis
- Tuberculosis (possibly)

During the administration of these hormones the physician must be on the alert to detect any toxic effects Psychic changes such as euphoria, hypomania or beginning depression may be serious and usually require cessation of the hormone Mentally unstable individuals are more likely to develop psychic changes Patients may develop glycosuria and those with diabetes mellitus are made worse although they are still amenable to control if adequate insulin is given Great care must be exercised in using these hormones in such patients and the hormone should be withdrawn as soon as practicable Usually the sugar metabolism returns to pre treatment status once the hormone is withdrawn Long-continued use of large doses will alter the electrolyte balance and cause retention of sodium while at the same time there is a loss of chloride and potassium When severe loss of potassium occurs, muscular weakness and paralysis may result Retention of sodium augments water retention and may produce or markedly increase edema fluid formation It is advisable to limit sodium chloride intake and increase the potassium intake of patients receiving treatment for periods longer than 2 weeks especially if large doses of corticotropin are used Potassium chloride given as enteric-coated tablets in a dose of 2 to 3 gm a day is usually sufficient to replenish any potassium loss and at the same time provide a mild diuretic action The moonface plethora striae supra clavicular and cervical pads of fat all observed in the Cushing syndrome may appear, as may acne, hirsutism and abnormal pigmentation of skin and nails especially in inflamed areas Less serious undesirable effects that may occur are decreased thyroid activity loss of calcium and increased nitrogen excretion Hypothyroidism should be corrected by adequate supplementary thyroid therapy, and the intake of calcium should be increased in patients receiving therapy for long periods

Hypertensive cardiovascular disease is made worse when these hormones are given and congestive heart failure may ensue or will be augmented if already present except in acute failure produced by rheumatic fever, where the beneficial effects of the hormone lead to im

PART II

BACTERIAL INFECTIOUS DISEASES

CHAPTER III

THE PNEUMONIAS AND ALLIED INFECTIONS

Description of the treatment of bacterial pneumonia will be discussed under three headings (1) *general methods* to be used when the etiology is any one of the several bacteria that can cause pneumonia, (2) *specific methods* available for use in the pneumonia caused by each of these causative bacteria and (3) methods of treatment of special symptoms and complications The same methods are to be applied whatever the anatomical distribution of the pneumonic process in the lung i e whether it is a lobar pneumonia or a bronchopneumonia (lobular pneumonia)

General Measures

For every patient with bacterial pneumonia the general treatment described in Chapter I should be applied *Isolation*, as described there is desirable Bed rest in a narrow hospital bed permitting easy adjustment to a semi sitting posture and ease in nursing procedure is essential With rare exceptions the patient almost always dyspneic should be placed in a semi sitting position and covered with small shoulder blankets in addition to regular blankets as needed to keep the body comfortably warm The open air or out of doors treatment of pneumonias formerly advocated by many and very generally used is no longer advised certainly not in colder climates A partly opened window will provide all necessary fresh air most physicians now consider cold air undesirable for patients with pneumonia As with few exceptions patients having pneumonia will be receiving oxygen the fresh air in the room and the

Pneumonia patients should receive twice daily a gently applied bed bath with cool sponging followed by powdering of the skin provided this does not prove unduly tiring or irritating If it does the routine should be modified However a good nurse can usually carry out these procedures in a way that is pleasant to the patient and not tiring

Urination and *defecation* should be carried on by in bed procedures If defecation does not occur daily or every second or third day a cleansing enema or a mild cathartic is the only measure needed unless there is abdominal distention This is frequent in pneumonia and should be watched for *diligently* since treatment of it in early stages is the best way to prevent its developing to such a degree as to impede respiration and make the patient very uncomfortable The treatment of abdominal *distension is described in Chapter 1 under Bowel Care*

Oxygen is advised for pneumonia patients especially if there is any cyanosis It can be given comfortably and adequately by using a small cellophane tent Oxygen is introduced into this tent so that it flows freely into all parts At some point near the oxygen tank is a water containing wash bottle connected so that the oxygen bubbles through the water Besides washing and humidifying the oxygen the water bottle has the further advantage of showing at once whether oxygen is flowing satisfactorily to the patient For most patients a flow of 5 to 7 liters of oxygen per minute is satisfactory The oxygen tent generally used in the past is not necessary it is complicated and difficult to operate and many patients dislike the feeling of being shut in by it Oxygen may be given by a nasal tube but most patients and physicians prefer the simple cellophane-type of mask and it seems entirely adequate The *more complicated close fitting masks have no great advantage over the* simple cellophane mask they are cumbersome and the patient is likely to object to them The oxygen concentration in the tent should be kept high at first 95 to 100 per cent but if it is to be continued longer than 12 hours it is better to reduce it to 50 to 60 per cent so as to avoid bronchial irritation

Nursing care is very important in the treatment of pneumonia and it should be continuous The intelligent nurse can do much to minimize fatigue during the many necessary procedures of treatment and to decrease the irritability and resistance that may be taking a large toll of the patient s strength and morale The nurse who is systematic moves slowly does things gently appears calm is sympathetic and cheerful and talks but little is ideal in the care of pneumonia patients The wise physician speedily replaces a nurse not having these qualities or one

room temperature should be regulated chiefly for the comfort of physicians nurses and family In hot weather measures to cool the room however are desirable

Diet should be fluid or semi solid and should include fruit juices Frequent feedings by the nurse should be scheduled with a feeding every 2 hours by day, less often at night unless the patient is awake A spouted feeding cup is helpful, otherwise a glass tube may be used Water should be given at regular intervals usually alternated with the 2 hour feedings, so that the patient will receive alternately food or water every hour If the patient is thirsty or seems dehydrated water should be given more frequently All food including water and other fluids should be taken very slowly with constant help from the nurse The total amount of fluid should be planned to prevent dehydration in a patient who necessarily is losing a very considerable amount of water by respiration or sweating or both in excess of that excreted by kidney and bowel Dryness of mucous membranes and shrinking of facial contours are indications of dehydration Urine output is a good index of the amount of fluid needed A 24-hour output of at least 2000 cc should be sought To attain this most patients will need a 24-hour fluid intake as great as 3000 cc and many will need more

If the patient fails to get the amount of fluid needed to prevent dehydration normal saline solution containing 5 per cent glucose should be given parenterally, preferably by the intravenous route to make up this deficiency By the intravenous route fluid must be given very slowly preferably by the drop method so as to avoid any overload of fluid in the circulation The physician must remember that the pneumonia patient is one in whom myocardial insufficiency is a potential complication to be guarded against

The patient with pneumonia unless cardiac congestive failure is present needs a considerable addition of sodium chloride to the fluids given him because the items in his dietary regime are likely to have a low content of salt, and pneumonia patients usually have as part of their disease a low blood content of sodium chloride For most patients 7 to 10 gm of sodium chloride should be added to the 24 hour intake of fluids but in such a way as not to make these fluids unpalatable For example it has been recommended that 1 gm of sodium chloride be added to a drink composed of orange juice, 200 cc dextrose 30 gm and water 400 cc Some salt may be added also to the drinking water However, salt should be restricted in the presence of a complicating cardiac congestive failure

after fever reaches normal and symptoms have decreased greatly Nausea is not infrequent after aureomycin but as a rule it is not marked enough to be very disturbing If it is penicillin should be substituted Occasionally, even penicillin does not prove satisfactory If so still another antibiotic should be used

Penicillin This is the drug of choice in the treatment of pneumococcic, *streptococcic, and staphylococcic pneumonia if the patient is* severely ill or has been untreated for several days because of delay in the recognition of the pneumonia Its use should be commenced as soon as possible after the diagnosis has been made It should be given intramuscularly or intravenously in aqueous solution by the technique described on page 22 An initial does should be given of 60 000 units followed by 30 000 units every 3 hours day and night until the crisis takes place or the temperature falls to normal by lysis Then the penicillin should be continued for 4 or 5 more days with omission of the night doses, penicillin in beeswax or procaine penicillin twice daily in 300 000 to 600 000 unit doses is excellent for this period After this penicillin should be omitted entirely unless a complication needing further penicillin therapy develops For sicker patients the dosage just indicated should be doubled, and for very ill patients it should be increased further so that 1 000 000 units are given each 24 hours as long as the temperature remains high Either the intramuscular or the intravenous route may be used Continuous flow of penicillin to give the same 24 hour total dosage is preferred by many, this can be accomplished by either the intramuscular or the intravenous route If at the end of 48 hours there is no definite improvement in the patient s condition the dosage being used should be doubled, and the diagnosis of the causative organism checked again to make sure that the pneumonia is not being caused by an organism unsusceptible to penicillin If the latter condition is found an antibiotic to which the organism is susceptible should be tried Intramuscular dosage of crystalline procaine penicillin 300 000 to 600 000 units every 12 hours may be used in the treatment of pneumonia when other routes of dosage using aqueous solutions cannot be carried out This should be done only if a dose of at least 100 000 units of soluble penicillin suspended with the procaine penicillin has been given to initiate the treatment This preparation may also be used to continue penicillin for 4 or 5 days after intramuscular or intravenous penicillin has been discontinued Penicillin is given orally only in the very mild cases and then only when it is impracticable or impossible to administer it by the parenteral route

who irritates the patient, remembering that personalities often clash without obvious cause

After the diagnosis has been made and treatment begun, the patient should be disturbed as little as possible by the physician and nurse Repeated physical examinations tire the patient, they should be made quickly and with the least possible change in the patient's position The physician should always watch for any sign of discomfort or undue fatigue, if they appear it is well to discontinue the examination As a rule, physical examination of the back once a day suffices, the heart region and the front of the chest may be examined more often if it seems desirable Frequent x raying is also fatiguing and should not be done unless the development of empyema is suspected Nursing care should be planned and so spaced as to give as little disturbance to the patient as possible

Specific Measures

Each pneumonia patient must have a prompt bacteriological diagnosis by microscopic study of the sputum and whenever possible, by cultural methods Sputum should be collected so as to be sure of obtaining a sample coughed up from the lung The patient should be instructed to that end by the physician who should personally collect the sputum specimen The specific measures to use in treatment depend on the etiological cause If a culture has been obtained, its susceptibility to the various specific measures may be determined, and this will serve as a guide in both the selection of the agent to use and the dosage

At present a number of antibiotics such as aureomycin, penicillin streptomycin and terramycin, are available This permits selection of the one usually most effective against a given causative bacteria and then a shift to another in case the one used at first is not effective or if toxic reactions are very prominent

Aureomycin For patients in the very early stages of pneumonia and for those only mildly ill, aureomycin is effective when the pneumonia is caused by pneumococci, staphlococci, streptococci, *Klebsiella pneumoniæ* (Friedlander's bacillus), or *B tularensis* Aureomycin has the advantage of effectiveness when given by mouth and so is particularly well suited for treating pneumonia patients in their homes If aureomycin does not give definite improvement particularly by lowering the fever penicillin should be substituted as described in the next section

Aureomycin should be given by mouth in doses of 0 25 gm every 4 to 6 hours this dose should be reduced to 0 .5 gm every 6 to 8 hours

In patients with pneumonia terramycin which can be obtained as the crystalline hydrochloride salt in 0 5 gm tablets or capsules should be given in an initial dose of 2 0 gm followed by 1 0 gm every 6 hours until the temperature is normal and symptoms have greatly abated or disappeared If toxic symptoms occur trial of dosage of 0 5 gm instead of 1 0 gm is advised

Sulfonamides If the patient with pneumococcic pneumonia is not very ill or if a sulfonamide is desired either sulfadiazine or sulfamerazine should be given as described on pp 19 21 If there is an unavoidable delay in beginning penicillin therapy the use of a sulfonamide should be begun as soon as the diagnosis is made and later when penicillin therapy is practicable a shift to penicillin should be made unless much improvement is in evidence At present with the availability of aureomycin there will be very little need for a sulfonamide

The dosage of sulfadiazine for a patient moderately ill with pneumococcic pneumonia should commence with an initial dose of gm followed by 1 gm every 4 hours day and night until the temperature has been normal for 48 hours dosage should be halved for an additional 4 hour period and then stopped For sicker patients these doses should be doubled During the period of sulfonamide dosage and the 4 hours after its cessation the urine should be kept alkaline by sodium bicarbonate given every 4 hours It should be tested for alkalinity frequently preferably at each voiding An initial dose of sodium bicarbonate 6 gm followed by 2 5 gm every 4 hours usually suffices to keep the urine alkaline Forcing fluids with sulfonamides is important

Some prefer sulfamerazine to sulfadiazine giving one half to three quarters of the doses advised in the preceding paragraph

If any toxic manifestations of sulfonamide therapy such as fever nausea and vomiting leukopenia jaundice nervous or mental disturbances hematuria with or without oliguria or anuria develop the sulfonamide in use should be stopped at once and if possible replaced by aureomycin terramycin or penicillin If this is not possible another sulfonamide should be substituted for the one that has caused the toxic manifestations Often when the sulfonamide is changed toxic symptoms do not recur If sulfonamides are used for pneumonia of streptococcic or staphylococcic etiology larger doses than those recommended for pneumococcic pneumonia are advised In these patients the use of penicillin if at all possible is strongly urged

Sulfonamides being given by mouth have an advantage over penicillin in which mouth dosage is still not entirely satisfactory They

The use of penicillin makes it possible although still difficult, to carry out treatment of pneumonia in a well-equipped home Well-trained nurses are needed throughout the 24-hour periods When the pneumonia is caused by streptococci or staphylococci large doses of penicillin are particularly important Somewhat smaller doses suffice for pneumonia of pneumococcic etiology when the patient is not seriously ill, these can be readily given at home

Streptomycin This is the drug to use in the treatment of pneumonia caused by *Klebsiella pneumoniæ* (Friedlander's bacillus), *Pasteurella tularensis*, *Pasteurella pestis*, *Hemophilus influenzæ*, and some strains of streptococcus and staphylococcus found to be resistant to penicillin Streptomycin is more toxic than penicillin and therefore its dosage needs to be planned so that enough streptomycin is given to obtain the needed antibacterial effect and yet not so much or for so long a period as to produce any of the more serious toxic effects These include its very occasional histamine like action and its more frequent neurotoxic action, particularly its toxic effect on the auditory (eighth) nerve Another inherent disadvantage in the therapeutic use of streptomycin is that fastness of the infecting organism develops readily making it important to use a dose large enough to inhibit or kill the infecting organism quickly All of this makes streptomycin a far less satisfactory therapeutic agent than penicillin and yet when the infecting organism is satisfactorily susceptible only to streptomycin as is true in the forms of pneumonia cited above it is the drug to be used

Streptomycin for the treatment of pneumonias caused by the organisms mentioned above should be given intravenously or intramuscularly continuously or intermittently as already described on page 25 It should be freshly dissolved in normal saline solution, 1 or 2 gm to 1000 cc and administered so that the patient receives a total of 2 to 4 gm each 24 hours until the temperature has become normal

Dihydrostreptomycin, given in the same doses and manner as streptomycin is as effective

Terramycin This is still another antibiotic available for the treatment of pneumonia, whether caused by gram positive cocci or by gram-negative bacilli Like aureomycin it is effective when given by mouth and consequently its usage should be that discussed in the paragraph on aureomycin As with aureomycin, its symptoms of toxicity are nausea, occasional vomiting, softer and sometimes more frequent bowel movements As a rule they will not necessitate discontinuing the use of terramycin

if it does occur it should be controlled by one of the drugs just mentioned

Restlessness, Insomnia, and Delerium Restlessness and insomnia are frequent in pneumonia, but much less so now than before the general use of sulfonamides and antibiotics If restlessness is using up the patient s strength it should be controlled preferably by a barbiturate as described on page 6 This also applies to insomnia If these are not effective codeine or morphine should be given It is important however to avoid continued deep sedation

If delerium develops and it may appear very abruptly, it may be con trolled by barbiturates but usually it requires the use of chloral hydrate paraldehyde codeine or morphine It should not be forgotten that delirium sometimes develops while the patient is under the influence of the sedative drug being given and may disappear if the depth of the sedation is materially lessened either by reduction of the dose or by a shift to a milder drug

Abdominal Distension or Tympanites If this develops the situa tion often becomes serious The distended abdomen hinders effective respiration and adds to the burden on the circulation it pushes the diaphragm up and lessens its excursion and it displaces the heart and compresses blood vessels in the abdomen Abdominal distension is usually caused by the great toxicity of the bacteria causing the pneu-monic process often with bacteremia it is an indication of the severity and seriousness of the illness It does not occur often when treatment with antibiotics has been begun early and is carried out efficiently If abdominal distension does develop it is well to increase the dosage of the penicillin or other antibiotic or to substitute them for a sulfonamide if the latter is being used As dilatation of the stomach may be causative of abdominal distension it is well to empty the stomach at once with a tube Sometimes the oxygen being given to the patient goes into the stomach and distends it a tube introduced into the stomach will relieve this Introduction of a rectal tube may help and should be tried pre-ceded by a cleansing enema Occasionally a Wagensteen suction appara tus is required to relieve abdominal distension In addition to these mechanical methods neostigmine or pitressin should be given as de scribed in Chapter I

When distension is moderate a so called carminative enema such as turpentine 2 to 4 cc beaten up with the white of an egg and added to a quart of water may be used Some advise the daily dose by mouth of a tablespoonful of castor oil

may be used when the pneumonia patient is only moderately ill, and continued if improvement is evident after 48 hours of use

Antisera The various antisera which were previously employed extensively and which require for their effective use detailed typing of the causative organism no longer need to be used Antibiotics, now available and already described give better results and are recommended for use in place of antisera In view of these conditions the therapeutic use of antisera in bacterial pneumonia will not be described in this book

Methods of Treatment of Special Symptoms and Complications

The treatment of bacterial pneumonia as already described has greatly reduced the incidence of special symptoms severe enough to need particular therapy and has similarly decreased the occurrence of complications This is particularly true when the diagnosis is made early in the development of the pneumonia and when treatment is begun immediately and is carried out skillfully and thoroughly

Cough In the majority of patients with bacterial pneumonia, cough is not a disturbing feature and needs no special treatment It is often a disturbing feature in non bacterial or viral pneumonia and its therapeutic management is described fully under that heading The same treatment should be applied when cough is disturbing and persistant in the patient with bacterial pneumonia

Pain Pleural pain is often severe in bacterial pneumonia and sometimes causes a sharp fall in blood pressure Treatment with an antibiotic is effective in decreasing pleural pain It should be controlled by a chest binder made of strong not easily stretched material applied over a layer of cotton with shoulder straps to keep it from slipping down and closed in front by straps with buckles to permit tight adjustment around the thorax If this is not effective codeine phosphate 60 mg, dihydromorphinone (Dilaudid) hydrochloride 1 5 to 2 0 mg methadone hydrochloride 5 to 10 mg meperidine (Demerol) hydrochloride, 0 1 gm, or morphine sulfate 8 mg should be given often enough to control pain Care should be taken to avoid amounts particularly of morphine, large enough to slow respiration below a normal rate Severe pleural pain causing a disturbing fall in blood pressure can be relieved at once by creating a small so called therapeutic pneumothorax or by blocking with procaine the intercostal nerve supply to the region Severe pain other than pleural pain occurs only infrequently in bacterial pneumonias,

plus other measures as indicated in early paragraphs of this section, is by far more important than any treatment applied after it develops

Pericarditis, Endocarditis, and Myocarditis These complications should be treated as described in Part XVIII The early recognition of their development is important With pericarditis any considerable accumulation of fluid should be diagnosed so that it may be removed by tapping if it is purulent, a solution of an antibiotic can be injected into the pericardial sac as described in the next paragraph on the treatment of empyema

Empyema Thoracis This is the complication of greatest incidence in bacterial pneumonia but like other complications, it is becoming fairly infrequent since the advent of chemotherapy, including antibiotics It should be watched for — particularly when the expected drop in temperature does not take place — by careful physical examination followed by x ray study as soon as its presence is suspected If it seems to be present a drainage needle or trochar should be introduced and the fluid usually purulent should be removed by suction drainage The causative bacterium should be demonstrated by study of stained smears and by culture Usually but not always the causative bacterium is the same as the one causing the pneumonia A different bacterium may be found however in the empyema fluid most often when this happens it is a streptococcus that is found The organism in the empyema fluid may be of a different susceptibility to the chemotherapeutic or antibiotic agent from that causative of the pneumonia This has a direct bearing on the selection of the proper antibiotic or chemotherapeutic agent to inject into the pleural space

The nature of the infecting organism and its susceptibility will determine whether to treat the empyema by injecting penicillin or other antibiotic into the pleural space

If the organism is susceptible to penicillin after the suction withdrawal of as much fluid as possible 50 000 units of penicillin should be injected into the pleural space and the intramuscular or intravenous injection of penicillin should be continued Pleural drainage and the injection of 50 000 units of penicillin dissolved in normal saline solution should be repeated daily as long as fluid recurs Some prefer to use 100 000 units instead of 50 000

If the organism is susceptible to streptomycin this instead of penicillin should be injected into the empyema cavity after withdrawal of the fluid 1 to gm of streptomycin dissolved in normal saline solution should be injected and repeated as described for penicillin Possibly

Circulatory Failure In some patients with bacterial pneumonia circulatory insufficiency, with or without auricular fibrillation, develops and causes congestive failure When this occurs it is usually in a patient with an antecedent heart disease and it should be treated with digitalis, diuretics et cetera as in any other patient with this form of heart disease, when decompensation becomes evident Except in this case, digitalis should not be used in patients with pneumonia

The more common form of circulatory insufficiency in pneumonia is the circulatory failure of acute infectious disease, or what is termed by some the shock syndrome of infectious disease In these cases there is usually no clinical evidence of pathological change in the heart, although in some there is actually an acute myocarditis Fortunately, this form of circulatory insufficiency occurs only infrequently under modern methods of treatment When it does occur therapy beyond that in use, as already described to inhibit the infection and the lesions caused by it has but little effect That digitalis drugs of any type should not be given to these patients is generally agreed So-called cardiac stimulants unfortunately bring about little if any improvement and, if pushed, may do actual harm If one is to be tried caffeine 0 6 to 1 gm or nikethamide (Coramine), 2 to 3 cc of a 25 per cent solution seems preferable Strychnine, metrazol or other forms of camphor are ineffectual Some recommend frequent doses of 0 2 to 0 3 cc of 1 1000 solution of epinephrine but many doubt its efficacy More physicians now advise the use of 0 1 to 0 4 cc of a 1 per cent solution of phenylephrine (Neo synephrine) hydrochloride administered subcutaneously or intramuscularly or 0 1 to 0 3 cc of this solution given intravenously, or 10 to 15 mg of the drug taken by mouth repeated as indicated but not more frequently than at 10 or 15 minute intervals Hydroxyamphetamine (Paredrine) hydrobromide may be tried 10 mg intramuscularly or 20 to 40 mg orally every 3 or 4 hours

Unless actual anemia or considerable dehydration is present intravenous blood plasma, or normal saline solution are not indicated They may even be harmful since with the exception of possible anemia or dehydration, blood volume in these patients is not decreased and to add to it by giving any liquid intravenously may put an added burden on the right heart The mechanism of this form of circulatory insufficiency has had much investigation It seems to be a form of shock that if it becomes well developed responds to no therapy, as has already been indicated It is a condition in which prevention by early and efficient treatment with an antibiotic (the selection being dependent on what bacterium is causative),

plus other measures as indicated in early paragraphs of this section, is by far more important than any treatment applied after it develops

Pericarditis, Endocarditis, and Myocarditis These complications should be treated as described in Part XVIII The early recognition of *their development is important* With pericarditis any considerable accumulation of fluid should be diagnosed so that it may be removed by tapping if it is purulent a solution of an antibiotic can be injected into the pericardial sac as described in the next paragraph on the treatment of empyema

Empyema Thoracis This is the complication of greatest incidence in bacterial pneumonia but like other complications it is becoming fairly infrequent since the advent of chemotherapy including antibiotics It should be watched for — particularly when the expected drop in temperature does not take place — by careful physical examination followed by x ray study as soon as its presence is suspected If it seems to be *present a drainage needle or trochar should be introduced* and the fluid usually purulent should be removed by suction drainage The causative bacterium should be demonstrated by study of stained smears and by culture Usually but not always the causative bacterium is the same as the one causing the pneumonia A different bacterium may be found however in the empyema fluid most often when this happens it is a streptococcus that is found The organism in the empyema fluid may be of a different susceptibility to the chemotherapeutic or antibiotic agent from that causative of the pneumonia This has a direct bearing on the selection of the proper antibiotic or chemotherapeutic agent to inject into the pleural space

The nature of the infecting organism and its susceptibility will determine whether to treat the empyema by injecting penicillin or other antibiotic into the pleural space

If the organism is susceptible to penicillin after the suction withdrawal of as much fluid as possible 50 000 units of penicillin should be injected into the pleural space and the intramuscular or intravenous injection of penicillin should be continued Pleural drainage and the injection of 50 000 units of penicillin dissolved in normal saline solution should be repeated daily as long as fluid recurs Some prefer to use 100 000 units instead of 50 000

If the organism is susceptible to streptomycin this instead of penicillin should be injected into the empyema cavity after withdrawal of the fluid 1 to gm of streptomycin dissolved in normal saline solution should be injected and repeated as described for penicillin Possibly

another antibiotic may be needed, depending on the infecting organism, but especially if it is a non gram staining one

If after several days of such treatment the purulent fluid continues to form in considerable quantity or if it becomes thickened and contains fibrin masses surgical drainage by rib resection should be instituted followed by the introduction of a drainage tube, the pleural space being washed out daily with an antibiotic introduced as before rib resection In a considerable proportion of patients who develop empyema thoracis and are treated by needle or trochar drainage and the introduction of an antibacterial rib resection will not be needed, the process will heal without it The use of Streptokinase Streptodornase in a dose of 200,000 units of the former and 60 000 units of the latter has shown promise when injected into cavities containing fibrin Usually 15 to 20 cc of saline containing the enzymes is injected into the cavity one or more times The enzymes effectively dissolve pus and prevent adhesions

Lung Abscess If this develops as a complication of bacterial pneumonia, it should be treated as described in the section on Diseases of the Lung With antibiotic and sulfonamide therapy lung abscess has become a rare complication of pneumonia

Acute Pulmonary Edema In pneumonia this complication can arise in one of two ways (1) caused by cardiac decompensation, (2) as an inflammatory edema When caused by cardiac decompensation acute pulmonary edema should be treated by immediate bleeding morphine, and a digitalis preparation as in any other form of cardiac decompensation (see p 707) If the pulmonary edema is an inflammatory edema, it will respond poorly to any therapy bleeding is not indicated for inflammatory edema Atropine sulfate 0 4 mg administered subcutaneously and repeated in 15 minutes if benefit is not apparent, may help With the first dose of atropine 8 mg of morphine sulfate should be given particularly if the patient is restless as is often the case Oxygen inhalation if not being used should be begun with the first signs of a developing edema

Anemia and/or Hypoproteinemia In a rare case of pneumonia these conditions may develop If the former should be evident blood transfusions are indicated if the latter occurs plasma or better human albumin should be given If both anemia and hypoproteinemia develop, transfusions with blood and plasma or human albumin should be given.

Polycythemia and Cyanosis If polycythemia develops bleeding is indicated If cyanosis is marked especially with distended neck veins, bleeding and continued oxygen inhalation are to be used Only infre-

quently however are these conditions marked enough to need such special treatment

Unresolved Pneumonia A condition called unresolved pneumonia used to be diagnosed frequently but in recent years the term has fallen into disuse What used to be so called usually turned out to be (1) empyema or (2) low grade cardiac failure with congestion that had gone unrecognized If a pneumonia does not seem to be responding adequately to proper therapy both of these conditions should be looked for and treated as outlined in preceding pages At the present time an other situation that might be called unresolved pneumonia is being seen occasionally in which there is a change in bacterial flora Initially an organism may be recovered that is susceptible to the antibacterial agent chosen while at the same time another organism not susceptible to the agent or agents being used has flourished and caused persistence of the infection It is good therapy therefore in any case of pneumonia not responding satisfactorily to carefully chosen therapy to obtain repeated examination of the sputum and to retest the sensitivity of any organisms recovered to the antibiotic being used A change in drugs may be neces sary to combat the new organisms isolated

BIBLIOGRAPHY

The Pneumonias and Allied Infections

1 APPLEBAUM E and LEFF W A Occurrence of Superinfections during Antibiotic (Penicillin) Therapy *Jour Amer Med Assoc* 1948 cxxxviii p 119
2 BRICKHOUSE I LEPPER M H STONE T E and DOWLING H F Soluble Sulfanomide Gantrisin (Gantrisin) *Am J Med*, 1949 ccxviii p 133
3 COLLINS H S GOCHE, T M and FINDLAND M Aureomycin Therapy of Non Pneumococcic and Nontuberculous Bacterial Pul monary Infections *Arch Int Med* 1949 LXXXIV p 875
4 DOWLING H F Treatment of Pneumococcic Pneumonia with Aureomycin *J Lab and Clin Med* 1950 xxxv p 15
5 KEEFER C S Alterations in Normal Bacterial Flora of Man and Secondary Infections during Antibiotic Therapy *Am J Med*, 1951 xi, p 665
6 REIMAN H A Infectious Diseases Fifteenth Annual Review of Significant Publications *Arch Int Med*, 1950 LXXXV p 156

7 SHORE, P D FLIPPIN, H F and REINHOLD J G 'Studies of Sulfadiazine Sulfamerazine (Sulforamides) Combination' *Am J Med* 1949 ccxviii p 80
8 TILLETT W S SHERRY S and READ T C 'Use of Streptokinase Streptodornase in Treatment of Postpneumonic Empyema,' *J Thor Surg*, 1951, xxi, p 275

CHAPTER IV

BACTERIAL INFECTIONS OTHER THAN PNEUMONIA

Local Infections

These infections may be caused by a variety of organisms The most common causative agents are the streptococcus staphylococcus, pneumococcus, and *Bacillus pyocyaneus* Infections in which these organisms and various anaerobic normally saphrophytic, bacteria are mixed are the most difficult to manage

Treatment should consist of early immobilization and protection of the infected part preferably by a light dressing rest in bed a light diet sufficient fluids to give a urinary output of 2000 cc daily and analgesics as required for pain Hot packs or hot soaks formerly so popular are of limited value but may prove soothing and restful to the patient Diabetes mellitus or other complicating diseases should receive careful management Depending on the sensitivity of the infecting organism a sulfonamide penicillin streptomycin or other appropriate sulfonamide or antibiotic should be given for their systemic effects If ulceration or localized skin infection exists, topical therapy in the form of bacitracin ointment, 500 units per gm usually gives best results Streptomycin 0 5 to 1 mg per cc in saline may be used but a local sensitivity reaction may develop Irrigation with tyrothricin 500 micrograms per cc if the surface area is not extensive and there is no likelihood of absorption is also useful but care must be exercised to avoid toxic renal effects from ab sorption Aureomycin or terramycin as a 3 per cent ointment may be applied in conjunction with the systemic therapy These are excellent and next to bacitracin ointment are least likely to cause local reactions Localized collection of pus should be incised and drained as soon as fluctuation is apparent

Septicemia Although most commonly resulting from a streptococcus invasion of the blood stream septicemia may result from the invasion of various other bacteria Most septicemias are a complication arising from a suppurative process elsewhere in the body

Treatment must be directed not only toward eliminating the organisms

from the blood stream but more especially toward the original source of the infection Since there is such a wide variety in the invading bacteria a sensitivity test to determine susceptibility to the various antibacterial agents should be made whenever possible in order that the most active agent may be employed in adequate concentration The local lesion, if such exists should be treated as described under Local Infections Bed rest, skillful nursing care abundant easily digested foods of the general type advised for typhoid fever and sufficient fluid to insure a daily urinary output of 2000 cc are indicated as general measures If circulatory failure exists the following measures may prove of limited assistance until specific therapy relieves the toxemia Blood plasma infusions or blood transfusions may be tried If blood for such transfusions can be obtained from individuals with a high immune serum titre against the invading organism, the value of the transfusion will be enhanced Whole-blood transfusions will prove most beneficial, also if there is concomitant anemia Caffeine and sodium benzoate, intramuscularly or intravenously 0.2 to 0.5 gm, phenylephrine (Neosynephrine) hydrochloride 0.5 to 5.0 mg intramuscularly hydroxyamphetamine (Paredrine) hydrobromide 5 to 10 mg intramuscularly or 20 to 40 mg orally, may be used Circulatory failure resulting from the toxemia of septicemia is most difficult to alleviate and usually responds poorly to any measures except those to relieve the toxemia

Specific antibacterial therapy in the form of penicillin streptomycin, or other appropriate antibiotic or an indicated sulfonamide should be started as soon as possible Penicillin is usually the agent of choice Dosage is regulated according to the degree of sensitivity of the invading organism Occasionally it is wise to combine the effects of penicillin with those of streptomycin depending on the type and sensitivity of the organism If the organism causing the septicemia is not sensitive to penicillin the antibiotic or sulfonamide to which it is sensitive is to be used instead

Complications of septicemia such as localized abscesses osteomyelitis meningitis hepatitis arthritis peritonitis endocarditis and pyelitis should receive the treatment described for the specific condition in addition to that for septicemia These conditions usually respond to the measures that prove effective against the original infection

FOCAL INFECTIONS Focal infections were formerly considered to be an important mechanism in many inflammatory conditions of muscles joints and various organs such as the kidney and the heart At the present time they are not assigned so important a role Local collections

of pus or low grade infections, however, can occasionally lead to serious disease and consequently it is wise to search for and remove a primary focus of infection whenever there appears to be a causal relationship Unfortunately there have been indiscriminate removal of tonsils teeth gall bladders and appendices cauterization of cervices and prostatic massages without any real indication for such therapy and usually without any help to the patient Occasionally real harm may result from these procedures such as the development of bacterial endocarditis following the removal of teeth in patients with cardiac lesions Badly infected teeth and tonsils should be removed but in the presence of congenital cardiac lesions or valvular involvement by rheumatic fever measures should be taken to prevent bacterial invasion of the blood stream before and after the operation Sulfadiazine in effective dosage begun 48 hours before and continued for 3 days after the operation or better penicillin given intramuscularly as penicillin procaine in aqueous suspension in amounts of 300 000 to 600 000 units every 24 hours administered for a similar length of time will prevent many complications Teeth should be removed with care preferably only one or two at a time Determined efforts should be made to get the patient into the best possible state of health by adequate rest plenty of fresh air and sunshine a nutritious diet correction of any anemia and removal of mental tension

Terminal Infections

Patients with serious or chronic diseases must be guarded against infections that might complicate their condition and bring about a terminal infection They should be shielded against exposures to weather over fatigue and contact with any sources of infection Care must be exercised by the physician not to carry an infection to them The patients should be isolated and wear masks to shield them from air borne infections whenever they are in contact with others and should be protected by a reverse isolation technique whereby they are shielded from others At the first indication of infection no matter how trivial the manifestations the patient should receive sulfonamide penicillin streptomycin or other antibiotic therapy in adequate amounts to control the infection promptly such treatment may prevent the infection from becoming a terminal one

CHAPTER V

STREPTOCOCCIC DISEASES

Erysipelas

Erysipelas is a streptococcal disease and so is amenable to the antibacterials effective against this bacterium Consequently the use of penicillin or other effective antibiotics or a sulfonamide is the most important part of its treatment

The general measures of treatment described in Chapter I should be applied All patients with erysipelas should have bed rest and if possible single-room isolation Isolation should be concerned chiefly with preventing the spread of the disease by those in attendance on the patient Surgeons and obstetricians in their work with other patients should not come into any contact with patients with erysipelas

Penicillin is preferable in the treatment of erysipelas It should be given as described on page 24 If for any reason penicillin cannot be given, one of the other effective antibiotics or a sulfonamide preferably sulfadiazine, should be used

For the skin lesion of erysipelas bacitracin ointment or wet packs of penicillin in normal saline solution 400 units per cc are advised and seem preferable to compresses of magnesium sulfate Local applications of cold compresses of 50 per cent solution of magnesium sulfate however are often comforting to the patient The former practice of applying to the spreading margins of the skin lesions such substances as ichthyol iodine silver nitrate collodion brilliant cresyl green or mercurochrome is no longer advised Treatment by ultra violet light and x ray also has become outmoded Erysipelas antitoxin convalescent serum and foreign protein therapy have been replaced by penicillin and sulfonamides

For local discomfort which sometimes amounts to actual pain codeine phosphate 30 mg with acetylsalicylic acid 0 6 gm should be given Hypnotics as described in Chapter I should be used when the patient is restless at night

Complications, frequently present before the use of antibacterials are now only occasional Infection of the eye especially from facial erysipelas is an important complication and should be treated at its onset by irrigation with aqueous penicillin solution containing preferably 250 and not over 500 units per cc every few hours

If there is anemia, blood transfusion should be given If inflammatory complications occur they should be treated by penicillin given intramuscularly or intravenously in increased dosage If local suppurative processes develop they should be treated surgically

Recurrences are frequent in erysipelas Often they originate by spread from local streptococcal lesions such as otitis media sinusitis and various local skin lesions other than erysipelas all of these should be treated in the appropriate ways during or subsequent to the presence of the erysipelas lesion

Erysipeloid

The lesion known as erysipeloid, a low grade indurated skin lesion should be treated vigorously with penicillin as described for erysipelas Erysipeloid occurring in conjunction with severe hypoalbuminemia as a complication of the nephrotic crisis responds to repeated intravenous administration of human serum albumin

Rheumatic Fever

At present rheumatic fever is considered to be a group of manifestations of the post streptococcal state This assumes an earlier streptococcal infection usually tonsillitis If with or following the tonsillitis there are any symptoms such as continued low grade fever increased blood sedimentation rate arthralgia or, especially disturbances in the electrocardiogram treatment for rheumatic fever should be begun immediately

General measures of treatment as described in Chapter I should be instituted *Complete bed rest is of great importance and should be* carried out for from 2 to 4 weeks after all signs of rheumatic fever have disappeared Evidence of continued activity of a rheumatic process is increased blood sedimentation rate but be sure that the increased rate is not being caused by salicylate therapy as it may be this relationship can be easily recognized by stopping the salicylates for a few days and

then repeating the determination of sedimentation rate If it is found that the sedimentation rate remains increased the patient should be considered to have continued activity of rheumatic fever, and treatment should be resumed for another period At present, continued bed rest remains the most effective measure of treatment particularly with regard to preventing or minimizing rheumatic involvement of the heart When bed rest has been continued in accordance with the procedures just mentioned, return to normal activity should be very gradual, each step being checked by pulse count an acceleration of pulse continued half an hour after ending the activity indicates that the return has been too rapid Any reappearance of symptoms of the rheumatic process is reason for a return to bed rest

From the point of view of infecting others isolation of the patient, except during the stage of acute streptococcal tonsillitis is not necessary It is highly important however especially during convalescence, to isolate the patient from contact with outsiders who so often bring to the rheumatic patient a new streptococcal upper respiratory tract infection which causes re exacerbation of the rheumatic fever process Such isolation is especially important in the management of children and young people with rheumatic heart disease

Salicylates remain our most useful agent in the treatment of rheumatic fever although unfortunately they appear to have almost no curative effect on rheumatic lesions of the heart

Salicylates should be given in the form of sodium salicylate or acetylsalicylic acid (aspirin) If gastric irritation results the former may be combined with an equal amount of sodium bicarbonate Aspirin may be given as an enteric coated tablet if it causes gastric irritation Salicylates should be given by mouth in dosages large enough to cause mild toxicity such as slight deafness and/or ringing in the ears, unless, before these appear there is very definite amelioration in fever and joint symptoms A good schedule to follow is to give sodium salicylate by mouth in a dose of 30 to 60 mg per pound of body weight every 24 hours The total dose should be divided into 4 or 6 doses and given every 3 or 4 hours when the patient is awake Sodium salicylate should be given well diluted with water or if it is given in powder or tablet form a full glass of water should be taken with each dose this also prevents gastric irritation Sodium bicarbonate in equal dosage is helpful but should be avoided if there is any evidence of cardiac failure Acetylsalicylic acid less irritating is preferable because it is productive of fewer unpleasant gastric symptoms and does not burden the body with extra sodium

For most patients the preceding schedule will suffice, but for those whose symptoms are not ameliorated larger doses of salicylates are needed these may be given by mouth unless toxic symptoms become too marked In that event particularly when the toxic symptoms are gastric in nature salicylates can be given by rectum Half an hour after a warm bland cleansing enema 5 to 15 gm of sodium salicylate, dissolved in warm cornstarch normal saline solution should be run slowly into the rectum once a day and allowed to remain there Salicylates can be given intravenously also using a dose of 10 0 gm of sodium salicylate dissolved in normal saline solution 2 to 3 times a day This intravenous method so often produced toxic symptoms that it has been almost abandoned after a rather limited use

The blood level of salicylates can be quantitated and the level used as a guide to salicylate dosage When an adequate blood level (35 mg per 100 cc) is not being maintained the level can be raised by increased dosage or the concomitant administration of para aminobenzoic acid giving an initial dose by mouth of 4 0 gm followed by 2 0 gm with each dose of salicylate To be successful this together with the salicylates should be given frequently throughout a 24 hour period and therefore it is a method not often of practical use The proprietary preparation of sodium salicylate 0 3 gm and sodium para-aminobenzoate 0 3 gm (Pabalate) may be used where such a combination is desirable Pabalate is also available in a sodium free form which contains para aminobenzoic acid and ammonium salicylate If no disturbing toxic symptoms develop salicylate therapy should be continued in the dosage in use until evidence of rheumatic disease activity disappears then it should be continued for two more weeks in progressively decreasing dosages If symptoms or signs of activity reappear salicylates should be given again Usually the withdrawal effect, consisting of the transient appearance of fever after the salicylates have been stopped can be avoided if the dose is reduced gradually Fever produced by this phenomenon subsides spontaneously in 3 or 4 days and does not recur

Allergic reactions to salicylates do occur and can be serious Patients with allergic diathesis should be given a small test dose of 0 3 gm If no reaction occurs within 3 hours the larger dose may be used If allergic reactions do occur the usual treatment for anaphylactic shock should be given

Patients who develop hemorrhages and those with a low prothrombin should be given vitamin K in a dose of 4 to 10 mg by mouth daily

If salicylates are poorly tolerated, or if they seem not satisfactorily

then repeating the determination of sedimentation rate If it is found that the sedimentation rate remains increased the patient should be considered to have continued activity of rheumatic fever, and treatment should be resumed for another period At present, continued bed rest remains the most effective measure of treatment, particularly with regard to preventing or minimizing rheumatic involvement of the heart When bed rest has been continued in accordance with the procedures just mentioned, return to normal activity should be very gradual, each step being checked by pulse count an acceleration of pulse continued half an hour after ending the activity indicates that the return has been too rapid Any reappearance of symptoms of the rheumatic process is reason for a return to bed rest

From the point of view of infecting others isolation of the patient, except during the stage of acute streptococcal tonsillitis, is not necessary It is highly important however especially during convalescence, to isolate the patient from contact with outsiders who so often bring to the rheumatic patient a new streptococcal upper respiratory tract infection which causes re exacerbation of the rheumatic fever process Such isolation is especially important in the management of children and young people with rheumatic heart disease

Salicylates remain our most useful agent in the treatment of rheumatic fever although, unfortunately they appear to have almost no curative effect on rheumatic lesions of the heart

Salicylates should be given in the form of sodium salicylate or acetylsalicylic acid (aspirin) If gastric irritation results the former may be combined with an equal amount of sodium bicarbonate Aspirin may be given as an enteric coated tablet if it causes gastric irritation Salicylates should be given by mouth in dosages large enough to cause mild toxicity such as slight deafness and/or ringing in the ears unless before these appear there is very definite amelioration in fever and joint symptoms A good schedule to follow is to give sodium salicylate by mouth in a dose of 30 to 60 mg per pound of body weight every 24 hours The total dose should be divided into 4 or 6 doses and given every 3 or 4 hours when the patient is awake Sodium salicylate should be given well diluted with water or if it is given in powder or tablet form a full glass of water should be taken with each dose this also prevents gastric irritation Sodium bicarbonate in equal dosage is helpful but should be avoided if there is any evidence of cardiac failure Acetylsalicylic acid less irritating is preferable because it is productive of fewer unpleasant gastric symptoms and does not burden the body with extra sodium

aqueous suspension intramuscularly once a day may be substituted for the oral dose if desired It is important that the penicillin be continued for at least 10 days if best results are to be obtained

Although a salicylate or amidopyrine usually gives satisfactory relief to most of the joint discomfort local applications are helpful The joints involved if persistingly uncomfortable, should be wrapped in cotton or wool batting On this oil of wintergreen (methyl salicylate) may be sprinkled after the joint has been rubbed gently with it That hot cloths saturated with Fuller s Solution (sodium bicarbonate) 25 gm tincture of opium (laudanum) 30 cc , glycerine 60 cc , and water 270 cc often decrease joint discomfort and seem to reduce swelling of the joints is an old clinical observation Chloroform liniment, gently rubbed over the joint followed by application of a hot cloth is also often comforting Heat by means of an electric pad or by the radiant heat from an electric bulb is often helpful Some patients prefer cold compresses or an ice bag over the painful joints

Immobilization of a joint by a well padded properly fitted splint under a firm bandage or the use of some form of light cast will reduce joint pain This is especially needed during periods of sleep since then the patient may move a joint and be awakened by the pain Without intermittent periods of passive motion of the joints however they may become immobile from adhesions

If there is much effusion into a joint tapping under aseptic precautions should be carried out Culture of the joint fluid should be made to detect the presence of bacteria If any are found, an antibacterial effective against the isolated organism should be injected as described for the treatment of gonococcal arthritis

The most important consideration in rheumatic fever treatment is the prevention of progression of the cardiac lesions, which unfortunately are an almost integral part of the disease For this, bed rest continued until all evidences of activity of the rheumatic disease process have dis appeared is of the utmost importance So long as there are tachycardia, signs of progressing valve le ion or continuance of changes in the elec trocardiograms rest should be continued even for months with very cautious return to out of bed activities Digitalis or other similar cardiac drugs should not be used, with the possible exception of quinidine or procaine amide (Pronestyl) if auricular fibrillation appears and persists If, despite efforts to prevent or retard progression of rheumatic lesions of the heart valvular heart disease with probably concomitant myocar dial lesions develops and progresses to cardiac insufficiency then treat

effective, amidopyrine (Pyramidon) may be used instead, without the accompanying sodium bicarbonate, in dosage not exceeding 0 5 to 1 0 gm every 4 hours The physician should remember however, that amidopyrine is potentially dangerous in the production of leucopenia and agranulocytosis to guard as far as possible, against the development of serious agranulocytosis while giving amidopyrine frequent leucocyte counts should be made and the drug stopped if the count falls to 4000 per cubic mm or less or if a marked fall in granulocytes appears Amidopyrine has been used frequently in rheumatic fever with excellent therapeutic results and no ensuing leucopenia

The statement that salicylates remain our most useful agent may need modification if the preliminary observations on the use of corticotropin (ACTH) and cortisone in the treatment of rheumatic fever are supported by further trial When corticotropin is given in a dose of 50 to 75 mg intramuscularly daily or cortisone by mouth in a dose of 50 to 100 mg twice daily, there is rapid disappearance of fever tachycardia polyarthritis, increased sedimentation rate, and abnormalities in the electrocardiogram The length of treatment varies with the individual patient, from 4 to 16 weeks, depending on the patient s response The hormone should be slowly reduced and the patient carefully evaluated during the withdrawal If symptoms reappear, the dosage must be increased While receiving these hormones the patient should be given potassium chloride in a dose of 1 to 3 gm daily in order to avoid potassium depletion and also to help remove fluid accumulation caused by the sodium retention The usual precautions recommended in Chapter 1 for patients receiving these hormones should be observed Obviously it will take extensive observation of many cases of rheumatic fever to justify any statement of its effect on that all important result of rheumatic fever on heart valves

So far no one of the antibacterial agents such as sulfonamides, penicillin or other antibiotic, is effective in rheumatic fever, and their use is not advised unless bacterial complications develop The same can be said of all sera and vaccines available at the present time It is now apparent however, that the prompt use of penicillin in these cases at the first sign of an upper respiratory infection due to the streptococcus will tend to prevent recurrences or relapses of the rheumatic fever Therefore in any rheumatic fever patient, at the first sign of a sore throat or an upper respiratory infection penicillin in a dose of 200 000 units 5 times a day by mouth is recommended Oral penicillin should be given while the stomach is empty A dose of 300,000 units of penicillin procaine in

300 000 to 600 000 units of penicillin for 4 or 5 days will in great probability protect others in contact with them including patients with rheumatic fever or rheumatic heart disease Penicillin in similar dosage by mouth may be given over long periods of time as a preventive measure Evidence so far gained strongly indicates that such therapy prevents rheumatic fever attacks in susceptible patients

Sydenham's Chorea

There is available no specific satisfactorily effective therapy for Sydenham's chorea Treatment consists in large part of general measures, especially measures designed to decrease motor activity in the patients this is done by various forms of symptomatic therapy and by good nursing

The greatest need of the patient with chorea is a decrease in the unco ordinated motor activity which is the chief clinical feature of Sydenham's chorea especially during its acute phase, it is a motor activity that prevents rest relaxation and sleep and wastes much of the patient's strength It can be reduced in part by nursing care including hydro therapy and in part by medicinal therapy These measures usually need persistence in application and long continuance

Every patient with chorea should be kept in bed in a single room visitors even members of the family and especially children should be excluded or greatly restricted in number and length of visits Except for the mildest case a nurse is necessary especially one who understands children and knows how to get along with them for the great majority of patients with chorea are children Such a nurse can do much to keep the patient reclining in bed with a minimum of motor activity the patient needs simple diversion devoid of excitement diversion the proper kind of nurse can supply The nurse can also carry out the necessary feeding procedures this may entail much skill to prevent the patient's uncontrolled often violently jerking muscle motions from hindering an adequate food intake With insistence on going slowly, some patients are able to feed themselves but most of them need to be fed by the nurse Many are unable to masticate solid food and can take only liquids Spouted feeding cups and drinking tubes are often required Some patients require nasal tube feeding Obviously the kind of food that can be taken depends on the severity of the choreic movements some can take only liquids others will be able to have a semi solid diet with

ment should be that described for any form of cardiac insufficiency

If acute pericarditis develops many believe that an increase in salicylates has a curative influence If there is pain in the precordial area, local use of an ice bag is often comforting, a hot application is sometimes preferred In the presence of pericardial effusion the rheumatic form of pericarditis does not become purulent unless secondarily infected with a pyogenic organism Consequently drainage in these patients is not usually a requirement The rheumatic effusion may become great enough however to raise the question of possible danger to the circulation from tamponade Actually this occurs so seldom that if tapping the pericardium is postponed until definite signs of tamponade appear, very rarely indeed will a rheumatic pericardial effusion be tapped, with very few exceptions the effusions reabsorb, and no serious cardiac damage results The adhesions that subsequently form usually do not in themselves hinder efficient cardiac function

If pneumonitis develops, it should receive in addition to the treatment being carried out for rheumatic fever that described under Nonbacterial Pneumonia If a pleural effusion develops it should be tapped for the same indications and in the way described in the section on Pleural Effusion

Persisting signs of tonsillar infection call for tonsillectomy Most prefer to operate during the quiescent period of rheumatic fever For 2 days before the day of and 2 days after the operation, penicillin or sulfadiazine should be given in usual dosage to prevent localization of pyogenic bacteria especially streptococci from the blood stream, their presence in the blood stream following tonsillectomy is to be expected Other foci of infection including apical infection of teeth should be surgically treated with the same use of antibacterials If there are valvular lesions in the heart this use of antibacterials is most important. To justify surgical treatment focal infections in rheumatic fever must be real not supposed The common removal of so called focal infections has had no beneficial effect on the course of rheumatic fever

Prevention of rheumatic fever to date has been limited to preventive or immediate treatment of streptococcal infection of the upper respiratory tract In the military forces in World War II prophylactic daily use of 0 5 gm of sulfadiazine was definitely effective in reducing the incidence of streptococcal infections including tonsillitis scarlet fever, and rheumatic fever In civil life such prophylaxis may well be applied in any epidemic like incidence of streptococcal infection If streptococcal carriers are detected by throat cultures, daily oral doses of

Tubocurarine chloride in a dose of ½ to ¾ unit per pound of body weight administered 1 to 3 times a day may be most helpful in serious cases The preparation of tubocurarine chloride in peanut oil and wax is frequently very useful in such cases because of its prolonged action Tubocurarine should be used only by those skilled in its administration and a syringe containing 1 cc of a 1 2000 solution of neostigmine (Prostigmine) should be readily available

As has been stated already there is no satisfactorily effective specific therapy for chorea Although acute chorea is considered to be an infectious disease little progress has been made in elucidating its specific etiology *Until that has been done it is unlikely that satisfactory specific therapy will be available* Although many believe that acute chorea is a streptococcic disease just as rheumatic fever is considered to be a streptococcic disease antibacterials such as sulfonamides and penicillin effective against streptococci have been disappointing in their therapeutic results even during the acute febrile phase of chorea They have been tried but reports of their effectiveness are not convincing Still with nothing better in the way of a specific therapy it seems advisable to give an antibiotic preferably penicillin to a patient with chorea during the active febrile period This is much the same attitude that is often taken at present with regard to the use of antibacterials in the treatment of acute, febrile rheumatic fever

As suggested in the preceding paragraph acute chorea has certain clinical resemblances to rheumatic fever Both behave as acute infectious diseases In each the streptococcus plays some role in etiology In each similar cardiac lesions develop very frequently in rheumatic fever less frequently in chorea These suggestively similar features indicate that chorea is very possibly a form of rheumatic fever with lesions predominantly in the nervous system and on this basis salicylates or amidopyrine have been used in the treatment of acute chorea as has been recommended for the treatment of rheumatic fever (see p 56) Considerable benefit has been claimed for such therapy but well studied cases with adequate controls are not available in sufficient number to justify a decision in regard to its merits

Arsenic long a favorite medicament for chorea especially in the form of Fowler s Solution given in continued and progressively increasing dosage has been largely abandoned since controlled cases without arsenic seemed to progress just as satisfactorily as those receiving arsenic Phenylethyl hydantoin (Nirvanol) once strongly commended is no longer advised its toxic reactions without which it seemed ineffective

additional needed liquids, still others will be able to take a solid diet The patients who must be fed, especially those with severe motor activity, need a balanced high calorie diet i e one with adequate protein, carbohydrate fat, and vitamin content and having not less than 1 5 gm of protein per kilogram of body weight It is also very important to include in the feeding enough fluid to prevent any dehydration With many chorea patients the feeding problem is the most difficult part of the treatment during the acute phase to meet it properly may require great ingenuity on the part of both physician and nurse As soon as possible the patient should be placed on a generous normally constituted diet, with ample vitamins, often purified vitamins should be given, especially B, C and D

Bed baths cooling sponges, or cool packs may be important adjuvants in decreasing the restlessness of patients with chorea For some, a warm continuous tub bath like those used for certain violent mental cases, has proved very effective A simple warm bath given once or twice a day may be helpful Some one of these forms of hydrotherapy is needed in the treatment of the majority of patients with chorea especially during the febrile period

A large daily dose 15 to 150 mg of pyridoxine hydrochloride is said to be of value some combine with it 30 to 60 mg of thiamine chloride

For motor restlessness a sedative is almost always needed For milder cases phenobarbital will suffice For more marked motor restlessness chloral hydrate is one of the most satisfactory sedatives for chorea patients and should be given by mouth in doses of 0 2 to 0 5 gm several times daily as needed If it is difficult to get the patient to take chloral hydrate by mouth it may be given by rectum in starch solution Diphenylhydantoin (Dilantin sodium) also is recommended for children of 4 years or less in doses of 30 mg twice a day for children of 4 to 6 years 0 1 to 0 2 gm a day in divided doses and for adults 0 3 gm a day in divided doses

If motor activity remains uncontrolled with this therapy, hyoscine hydrobromide in 0 4 to 0 6 mg doses may be given subcutaneously This failing mephenesin (Tolserol) 1 5 to 4 0 gm by mouth daily in divided doses, may be helpful Anesthesia with tribromoethanol (avertin with amylene hydrate), ether in oil by rectum or even respiratory anesthesia may be required to control very violent choreiform movements It is possible to control violent choreiform restlessness by avertin anesthesia continued for 4 or 5 hours and repeated several times after a few hours' interval, until finally relaxation and normal sleep ensue

Tubocurarine chloride in a dose of $\frac{1}{2}$ to $\frac{3}{4}$ unit per pound of body weight administered 1 to 3 times a day may be most helpful in serious cases The preparation of tubocurarine chloride in peanut oil and wax is frequently very useful in such cases because of its prolonged action Tubocurarine should be used only by those skilled in its administration, and a syringe containing 1 cc of a 1 2000 solution of neostigmine (Prostigmine) should be readily available

As has been stated already there is no satisfactorily effective specific therapy for chorea Although acute chorea is considered to be an infectious disease, little progress has been made in elucidating its specific etiology Until that has been done it is unlikely that satisfactory specific therapy will be available Although many believe that acute chorea is a streptococcic disease just as rheumatic fever is considered to be a streptococcic disease antibacterials such as sulfonamides and penicillin effective against streptococci have been disappointing in their therapeutic results even during the acute febrile phase of chorea They have been tried but reports of their effectiveness are not convincing Still with nothing better in the way of a specific therapy it seems advisable to give an antibiotic preferably penicillin to a patient with chorea during the active febrile period This is much the same attitude that is often taken at present with regard to the use of antibacterials in the treatment of acute febrile rheumatic fever

As suggested in the preceding paragraph acute chorea has certain clinical resemblances to rheumatic fever Both behave as acute infectious diseases In each the streptococcus plays some role in etiology In each similar cardiac lesions develop very frequently in rheumatic fever less frequently in chorea These suggestively similar features indicate that chorea is very possibly a form of rheumatic fever with lesions predominantly in the nervous system and on this basis salicylates or amidopyrine have been used in the treatment of acute chorea as has been recommended for the treatment of rheumatic fever (see p 56) Considerable benefit has been claimed for such therapy but well studied cases with adequate controls are not available in sufficient number to justify a decision in regard to its merits

Arsenic long a favorite medicament for chorea especially in the form of Fowler s Solution given in continued and progressively increasing dosage has been largely abandoned since controlled cases without arsenic seemed to progress just as satisfactorily as those receiving arsenic Phenylethyl hydantoin (Nirvanol) once strongly commended is no longer advised its toxic reactions, without which it seemed ineffective

are considered dangerous enough to justify eliminating it from the therapy of chorea

Hyperpyrexic treatment either by means of intravenous doses of typhoid paratyphoid vaccine or by using a Kettering hypertherm or short-wave diathermy is said to be very beneficial in the treatment of chorea in its acute phase and recent work indicates that hyperpyrexia is by far the treatment of choice It can be used in the presence of acute arthritis myocarditis or endocarditis It appears especially effective, since after a full course recurrences were rarely seen If a hypertherm is not available the use of bacterial vaccine hyperthermia presents no great difficulty the proper dose of a vaccine containing 1000 million typhoid and 750 million each of paratyphoid A and B is soon found by increasing from an initial dose of 0 1 cc to the dose needed to maintain for at least 2 hours a febrile reaction reaching 104° to 105 F Such febrile reactions can be repeated daily for 8 consecutive days or less frequently as seems best for the patient

As already intimated usually the treatment of chorea particularly the nursing care and sedation must be continued for a long time, usually for weeks As choreic movements lessen the patient can be allowed to sit up, then to move about and finally to have restricted supervised exercise At this stage gradual return to contact with other children is advised It is important to reduce excitement as far as possible unless restricted, the patients usually children are likely to play too hard and to become easily excited When this happens return of choreic movements is likely Convalescense is very often a prolonged process

With persisting choreiform movements a form of chronic chorea may develop This will require prolonged nursing and educational care The help of a neuropsychiatrist will often be needed in the management of these patients This form of chorea often progresses most satisfactorily in a sanitorium where similar patients are being cared for

If cardiac complications develop as they may they are to be treated as described under Rheumatic Fever Any localized infections need prompt treatment Teeth need extra care as there is an increased tendency to cavitation If anemia develops iron is indicated

SCARLET FEVER

In treating scarlet fever the physician must remember that it is a disease in which two factors are causative of symptoms the toxic and the septic and each needs consideration in treatment For convenience the

treatment of scarlet fever will be discussed under seven headings (1) general measures, including isolation (2) throat and ear care (3) skin care, (4) use of antibacterial therapy (5) use of antitoxin convalescent serum and gamma globulin (6) treatment of complications, and (7) prophylaxis prevention A rational treatment should be composed of a combination of many of the procedures discussed under these headings

General Measures Including Isolation

The general measures described in Chapter I should be applied in the treatment of scarlet fever of all degrees of severity Bed rest during the febrile period should be enforced Single room isolation is desirable although not necessary when precaution can be taken against contact transmission from patient to patient by a third party or when children in the family can be sent away from the home

Isolation The time required or advised for isolation of scarlet fever patients with no discharging local suppuration varies from a minimum of 1 week in some localities to 5 weeks in others

New York City includes scarlet fever as a form of streptococcal sore throat and for uncomplicated cases requires isolation until the mucous membrane of nose and throat appear normal but for not less than 7 days after onset of the disease For complicated cases (discharging nose and ears mastoiditis enlarged suppurating lymph nodes pneumonia) isolation is required until recovery if the complication persists for 45 days from onset however cultures should be made and if two taken not less than 24 hours apart are negative the case may be discharged

The Massachusetts Department of Public Health gives the following directions for isolation *Uncomplicated Cases* Adults 2 weeks children 3 weeks each from date of appearance of rash Examine nose throat and ears for existence of discharge or inflammation before designating case uncomplicated If upper respiratory-tract symptoms appear during month after release from isolation re establish isolation precautions *Complicated Cases* 4 weeks at least and thereafter until abnormal discharge has ceased swollen lymph nodes have subsided or 3 successive cultures of abnormal discharge taken at 24 hour intervals have been found free from hemolytic streptococci

Diet and Fluid Intake

There are two schools of thought regarding diet and fluid intake (1) giving large amounts of fluid including water and fruit juices with

restriction of sodium chloride and protein, (2) giving an easily digestible diet, rich in protein carbohydrate and fruit juices, with such additions of water as are needed to prevent dehydration — in other words a diet that is appropriate to any febrile infectious disease The first of the two dietary plans was based on the idea that such diet and fluid intake were needed to prevent the development of nephritis (Bright's disease) This view is no longer held by most physicians with experience in treating scarlet fever and the second, more liberal, diet without excess fluid is now generally used

Throat and Ear Care

Since, as already indicated above, scarlet fever is considered to be a form of streptococcal sore throat throat symptoms should receive prompt therapeutic attention such as would be given to any patient with acute tonsillitis If the throat is only mildly inflamed local therapy, with occasional irrigation of nose and throat with a slightly alkaline warm cleansing douche or with warm normal saline solution, is all that is needed If it is more severely inflamed more frequent irrigation is desirable and penicillin should be given as described in the section on Acute Tonsillitis Antiseptic solutions either for gargling or for irrigating, are not very helpful and they are not generally advised If cervical adenitis develops, an ice bag should be applied locally, penicillin already in use, should be given in increased dosage and if suppuration develops surgical drainage is indicated

Daily otoscopic examination of the ears is desirable, with prompt puncture of the ear drum if otitis media develops Examination for mastoid tenderness and asking about pain in or back of, the ear should be a daily procedure if mastoid tenderness or pain develops mastoiditis is probable and a surgical consultation is advised since prompt drainage may be very important to a prompt cure or at any rate to the prevention of chronic complications

Skin Care

When desquamation takes place, the application of petrolatum (vaseline) to the desquamating surfaces is comforting and will usually prevent or reduce any itching or burning sensation If the latter persists and

becomes severe tripelennamine (Pyribenzamine) hydrochloride should be given by mouth in doses of 50 mg repeated at intervals as needed or applied as a 2 per cent ointment If furunculosis erysipelas or other inflammatory lesions develop these should be treated

Use of Antibacterial Therapy

Antibacterials are effective only against the septic streptococcic factors of the disease Penicillin is preferred and should be used instead of a sulfonamide If used it should be continued for 7 to 10 days and, if there are suppurative complications for a longer time depending on the observed effect of the drug on these complications If penicillin cannot be used aureomycin or sulfadiazine in adequate dosage may be substituted Very mild cases exhibiting no complications frequently do not require antibacterial therapy In spite of adequate antibiotic therapy there still remains the possibility of serious sequelae to this infection

Use of Antitoxin, Convalescent Serum and Gamma Globulin

These therapeutic agents are effective only against the toxic factors of scarlet fever In mild cases these sera are not needed In moderately severe to severe cases with rash it is advisable to neutralize the circulating toxin with either scarlet-fever antitoxin or convalescent serum Convalescent serum is at present preferred to scarlet fever antitoxin since the former causes no toxic reactions especially serum sickness which unfortunately are of frequent occurrence following antitoxin and which may be serious Convalescent serum may be given intramuscularly or intravenously preferably the latter in doses of 20 cc for moderately severe cases 60 cc for severe cases when the patient weighs less than 50 pounds If the patient weighs more than 50 pounds the dose should be 40 cc for moderately severe cases 100 cc for severe ones If toxic symptoms persist the doses should be repeated at 12 to 24 hour intervals until these symptoms decrease markedly or disappear Fall in temperature and fading of the rash are evidences of a satisfactory antitoxic effect

If scarlet fever antitoxin is to be used the patient must be tested for sensitivity to horse serum if the test is positive desensitization as described for Diphtheria must be carried out After these preliminaries

antitoxin should be given intramuscularly in doses of 8000 units in cases of moderate severity and 16 000 units for patients who are severely ill, these doses should be doubled for patients over 50 pounds in weight In very severe cases the intravenous route may be used These doses should be repeated as just described for the use of convalescent serum It is to be remembered that these sera have no effect on septic complications, which require treatment with antibacterial agents, preferably penicillin as described in the preceding section

Gamma globulin has been used in the eruptive stage of scarlet fever with reports of benefit Possibly further trial may prove it of value in the treatment of the toxic phase of scarlet fever even if it is found very effective, the cost may be too great for any extensive use

Treatment of Complications

Except for acute nephritis and myocardial lesions the complications of scarlet fever are almost entirely of an inflammatory nature and are usually of streptococcic etiology They include acute cervical adenitis acute parotitis otitis media acute mastoiditis (sometimes becoming chronic) acute sinusitis bronchitis, bronchopneumonia, lobar pneumonia, empyema thoracis acute pericarditis acute vegetative endocarditis, acute pancreatitis acute hepatitis streptococcic septicemia acute (sometimes purulent) arthritis acute osteomyelitis, peritonitis, acute meningitis brain abscess, and thrombophlebitis

Some of these lesions such as the polyarthritis and cardiac lesions are similar, if not identical to those occuring in rheumatic fever and should be treated in the same way Acute nephritis in scarlet fever is treated just as any other form of acute nephritis the early use of penicillin seems advisable In all of the other complications treatment should consist of increased dosage of penicillin with surgical drainage if the process becomes seropurulent or purulent and in addition the local injection of penicillin With the use of penicillin in the treatment of all except the very mild cases of scarlet fever the incidence of complications has greatly decreased

Prophylaxis Prevention

When large numbers of young people come together, as in military service a mass prophylactic dose of 0 5 to 1 gm of sulfadiazine daily,

over a period of weeks or 100 000 to 300 000 units of penicillin by mouth daily for a similar period has been effective in greatly reducing the incidence of acute tonsillitis rheumatic fever and scarlet fever. This method should be applied also to streptococcus carriers.

Individuals who have been exposed to scarlet fever should have their immunity determined by a Dick test. This is done by injecting intradermally 0 1 cc of a standardized solution of scarlet fever toxin. Twenty-four hours later the susceptible will show a localized area of erythema at least 10 mm in diameter; these persons are called Dick positive. If the test is negative, the danger of developing scarlet fever is very slight. Those whose test is positive are likely to develop scarlet fever if exposed to patients who have it. Rigid isolation of the susceptible from scarlet-fever patients should be practiced and steps should be taken to develop in them as much immunity as possible. For this convalescent serum or scarlet fever toxin should be given. The latter has the disadvantage of frequently causing severe uncomfortable reactions and for this reason even though the resultant immunity is more marked and lasting its use has been limited in the most part to nurses in scarlet fever wards who give positive Dick tests and who are necessarily exposed to scarlet fever. If there is doubt about imposing rigid isolation or if exposure already has taken place convalescent serum is advised. The following plan of dosage of scarlet fever toxin has been advised each dose given subcutaneously in alternate arms at weekly intervals 1st injection 650 skin test doses 2nd injection 2 500 skin test doses 3rd injection 10 000 skin test doses 4th injection 30 000 skin test doses 5th injection 100 000 to 120 000 skin test doses. This should convert a positive Dick test to a negative one [illegible] weeks after the last injection. For immunization with convalescent serum 10 cc intramuscularly is advised for very small children and [illegible]0 cc for older children and adults repeated after 10 to 14 days and again if subsequent exposure occurs. Temporary passive immunity also is possible from injections of scarlet fever antitoxin in doses as advised for treatment of milder cases. None of these immunizing methods is entirely satisfactory after all they are protective only against the toxic phase of scarlet fever and have no effect on the causative streptococci. Also the Dick test does not always give entirely certain evidence for or against susceptibility to scarlet fever before or after immunizing procedures. Consequently the present tendency is to rely chiefly on isolation procedures.

ACUTE TONSILLITIS

Acute inflammation of the tonsils, although self limiting, may be serious and can lead to dangerous complications Treatment must be directed toward conserving the patient s strength, avoidance of mucous membrane irritation and final resolution of the infection Bed rest is of prime importance and should be instituted promptly Precautions should be taken to prevent spread of the infection to other persons The patient should be instructed to avoid conversation or any other activity likely to be irritating to the mucous membranes or to bring on fatigue The diet should be liquid or of soft solids depending on the degree of inflammation and the desires of the patient It is usually wiser to begin with an all-liquid diet and to add soft solids as the inflammation and pain subside When swallowing is painful an anesthetic lozenge containing nupercaine (Nuporals) permitted to dissolve in the mouth before feeding may serve indirectly to increase the patient s intake of needed fluids and food Fluids should be taken in sufficient amounts to maintain a urinary output of from 1500 to 2000 cc a day but they should not be forced in large amounts

Pain may be controlled with acetylsalicylic acid, with phenacetin, or, if pain is severe and cough is a factor with a combination of these drugs with codeine phosphate or with codeine alone Occasionally an apprehensive patient responds better to a combination of these analgesics with a barbiturate such as phenobarbital If depression is a factor as is often the case in infections of this type the combination of the analgesic with a central nervous stimulant such as caffeine or amphetamine (Benzedrine) is indicated as described in Chapter I

Throat irrigations every 2 or 3 hours with physiological saline made alkaline with sodium bicarbonate or with a 10 per cent glucose solution are helpful in relieving the irritation and pain Both solutions should be as warm as can be tolerated Likewise steam inhaled from a pitcher of boiling water around which a newspaper or towel has been folded so as to direct most of the steam toward the patient will prevent dryness and consequent irritation of the mucous membranes Tincture of benzoin (4 cc to a quart of water) may be added to the boiling water to increase the efficacy of this treatment The same result may be attained with an electrically operated inhalator which blows steam into the patient s face The humidity of the room must be kept high if irritation is to be avoided An ice bag applied to the neck may give some comfort and is worth a trial Some patients prefer a hot application to a cold one

Local applications formerly so extensively employed are of questionable value Silver nitrate 10 to 50 per cent, applied to the crypts bearing surfaces of the faucial tonsils is believed by some to hasten healing Others consider this too drastic Care must be taken to prevent the silver nitrate from coming in contact with non inflamed areas of the pharyngeal wall and especially the laryngeal structures

Penicillin applied topically in the form of powder, sprays gums lozenges and aerosol or irrigating solutions is of value There is some possibility however of bacterial resistance developing before the infection is completely controlled Sulfonamides formerly used extensively for local throat applications are now considered much less preferable than penicillin preparations Generally speaking if the infection is sufficiently severe to warrant the use of antibiotic agents they should be given systematically in the doses and manner outlined on page 22 For exceedingly severe infections systemic therapy with large doses of penicillin 100 000 units intravenously or intramuscularly every 2 hours should be given

Repeated acute infections or chronic infections and irritations of the tonsils especially if accompanied by enlargement of the cervical lymph nodes, are indications warranting surgical removal of the tonsils Chronic tonsillar infection following repeated acute attacks leads to involvement of other portions of Waldeyer s ring with consequent pharyngeal lymphoid hyperplasia, chronic upper respiratory tract irritation and auditory impairment Surgical removal of the tonsils and adenoids usually clears up most of the symptoms but in some cases generalized lymphoid hyperplasia especially around the openings of the eustachian tubes may require radiation therapy to destroy the excess lymphoid tissue before auditory impairment is relieved

BIBLIOGRAPHY

Rheumatic Fever

1 DINGLE J H and RAMMELKAMP C H Prevention of Rheumatic Fever *U S Armed Forces Med J* 1951 II p 607

2 MASSELL B F Salicylates Hormones and Penicillin in Treatment of Rheumatic Fever *Med Clin No Amer*, 1950 XXXIV p 1419

3 MASSELL B F STURGIS G P KNOBLOCH J D STREEPER, R B HALL T N and NORCROSS P Prevention of Rheumatic Fever by Prompt Penicillin Therapy of Hemolytic Streptococcic Respiratory Infections *Jour Amer Med Assoc*, 1951, cxlvi, p 1469

Scarlet Fever

4 WEINSTEIN L BACHRACH L and BAYER N Observations on Development of Rheumatic Fever and Glomerulonephritis in Cases of Scarlet Fever Treated with Penicillin *N E J Med*, 1950 ccxlii, p 1002

CHAPTER VI

OTHER COCCIC AND BACILLUS HEMOPHILUS DISEASES

Cerebrospinal Fever

Meningococcus Meningitis. Early diagnosis and prompt treatment are essential for the successful management of meningococcal meningitis. The patient should be isolated at once and strict isolation technique established and maintained until meningococci are no longer present in the nasopharynx. The family and all immediate contacts should be quarantined until proved not to be carriers. Whenever possible the patient should be placed in a cool, darkened solitary room, away from any noise distraction, or possible source of irritation. Prompt skilled nursing is an essential part of treatment.

A liquid diet is advisable in the acute stage to be supplemented by soft solids as the patient improves. Feeding at frequent intervals is desirable, and when necessary should be through a nasal or stomach tube. Fluids are to be given in sufficient amount to avoid dehydration. A daily urinary output of from 1500 to 2000 cc is a good index that sufficient fluid is being given. Intravenous saline or glucose and saline solution should be given when because of nausea, vomiting or dulled sensorium insufficient fluid intake by mouth is leading to dehydration.

The severe headache and muscle pains so often present are difficult to manage. Frequently lumbar or cisternal puncture with the gradual withdrawal of sufficient fluid to reduce the cerebrospinal fluid pressure to normal will give considerable relief. Analgesics such as acetylsalicylic acid and phenacetin are usually not very effective. Because of their antispasmotic effect in addition to their potent analgesic effect better results will be obtained with meperidine (Demerol) hydrochloride 100 mg or methadone hydrochloride 5 to 10 mg given hypodermically and repeated at 3 hour intervals if needed. Morphine sulphate 8 mg

administered hypodermically every 4 hours also will give excellent results

Uncomfortable chilly sensations and chills can be combated with hot liquids and warm but light weight bed clothing The use of an electrically regulated blanket or electric heating pad is also effective For the hot highly febrile patient cooling sponge baths will stimulate circulation and relax nervous tension in addition to lowering the fever If agitation, excitement or delerium is present, the bed should have side boards and a barbiturate sedative should be given, usually one of the longer-acting variety such as phenobarbital is to be preferred

Specific therapy should be instituted promptly Sulfadiazine and penicillin should be given A 5 per cent solution of sodium sulfadiazine in normal saline, given intravenously and followed by the usual oral dosage of sulfadiazine is recommended A blood level of at least 12 to 20 mg per cent should be maintained In severely ill patients the intravenous use of the sodium salt should be repeated at 6 hour intervals until definite clinical improvement is noted, then mouth dosage of sulfadiazine can be started Since with sulfadiazine approximately 60 per cent of the blood level is found in the cerebrospinal fluid intrathecal administration of sulfadiazine is usually not indicated In the majority of patients response should be prompt with a fall in temperature to normal within 48 hours Sulfadiazine should be continued until the temperature has been normal for at least 5 to 7 days Lumbar puncture is indicated for intrathecal therapy and to relieve symptoms of increased intracranial pressure

Penicillin by itself is not so satisfactory in its effects as a sulfonamide but it should be given with the sulfonamide If the sulfonamide causes toxic effects penicillin should be substituted Penicillin should be given in the same dosage and manner as for other infectious diseases (see page 22) The continuous intravenous route is recommended for severe infections to be followed by the intermittent intravenous or intramuscular route as the condition of the patient improves It is essential that penicillin be given intrathecally as well as intravenously For this purpose a dose of 20 000 units dissolved in 10 cc of physiological saline is to be given after the withdrawal of 15 to o cc of cerebrospinal fluid, this is to be followed by from 2 to 5 doses depending on indications of 10 000 to 15 000 units at 12 hour intervals

The various complications should have in addition to the plan of treatment just described such local treatments as are appropriate to the complication, these are described under their various headings

Antimeningococcic serum seems to add very little to the effectiveness of treatment and at present is rarely used — in some clinics it is never used. Occasionally in the highly toxic type of infection it is of possible value. If used it is to be administered intravenously after preliminary sensitivity tests give negative reactions in a dose of from 50 to 300 cc or more, well diluted with 10 per cent glucose solution. Intrathecally a dose of 20 to 40 cc is recommended in addition to the intravenous dose.

If signs and symptoms of severe adrenal cortical damage (Waterhouse-Friderichsen syndrome) appear prompt administration of desoxycorticosterone, cortisone or adrenal cortical extract accompanied by adequate salt intake parenterally to replenish that lost by the kidney as described under treatment for the crisis of Addison's disease is recommended in addition to vigorous sulfonamide and penicillin therapy.

Influenzal (Hemophilus Influenzae, Pfeiffer's Bacillus) Meningitis

At present, an effective treatment for hemophilus influenza meningitis is streptomycin alone in mild to moderate cases supplemented by sulfadiazine in severe cases. The use of specific antiserum probably is not necessary.

Streptomycin. In mild cases 8 doses of 0.25 gm (250 000 units) of streptomycin should be given intramuscularly at 3 hour intervals in each 24 hours. For more severe cases 2 or 3 times that amount may need to be given. Streptomycin may have to be continued for a week or even longer. Many advocate the use of intraspinal therapy with streptomycin in doses of 10 to 25 mg every 24 hours in addition to the intramuscular dosage. Dihydrostreptomycin can be used instead of streptomycin.

There is evidence, however, that routine intraspinal streptomycin is not necessary; in fact it may even be the cause of some of the residua that are being reported now that infants and children are surviving under this new form of therapy. These complications consist of such lesions as hydrocephalus, extremity pareses and paralyses, cerebral thromboses, nerve deafness and so on. The same complications may result, however, from the disease itself.

Today most pediatricians advise a sulfonamide, preferably sulfadiazine, in addition to streptomycin. The initial dose of sulfadiazine may be given intravenously in the form of a 5 per cent solution of 5 gm of the

sodium salt For children the initial dose should be 1 cc of a 5 per cent solution per pound of body weight Subsequent dosage may be computed on a basis of 60 mg per pound of body weight per day, and may be divided into 6 doses and given by mouth at 4-hour intervals Some advise withholding the sulfonamide therapy for 72 hours, using streptomycin alone Then, if the response is not satisfactory, or if the patient becomes worse, they add sulfadiazine and in some critical instances also give the specific rabbit antiserum especially when the infection is proved to be caused by the type B organism A dose of 50 to 100 mg of antiserum is recommended as an initial dose Subsequent dosage is determined by the presence or absence of antibody in the patient's serum the following day and by the level of glucose in the spinal fluid Spinal-fluid glucose levels below 50 mg per 100 cc require a dose of 50 to 75 mg of serum for levels of 50 mg or more 25 to 50 mg of serum should be given A maintenance dose of serum is usually 25 to 75 mg daily

Because of the tendency toward relapse the streptomycin may have to be given for as long as 3 weeks When sulfadiazine is used in addition to streptomycin, it should be continued in regular dosage for 2 weeks after the streptomycin has been stopped

Aureomycin This antibiotic appears also to give excellent results when given by mouth in doses of 60 mg per kilogram of body weight daily the dose being divided and given every 6 hours If further reports confirm this aureomycin will be preferable to streptomycin because of its lesser toxicity Some suggest an initial dose of 1 0 gm of aureomycin given intravenously

Terramycin Like aureomycin terramycin gives good results in the management of this disease It is given in the same manner and dosage as aureomycin

Chloramphenicol This antibiotic also gives good results in this form of meningitis It is given in the same dosage as advised for aureomycin but its use should be restricted to those cases which do not respond well to other antibiotics

Now that there are several antibiotics to choose from better results with fewer toxic reactions may be expected

It is well to remember that secondary invasion by bacteria such as staphylococci particularly in the nose and throat is not uncommon in this disease When this occurs it should be treated vigorously with full doses of penicillin Penicillin on the other hand is ineffective against *Hemophilus influenzae*

GONOCOCCUS INFECTIONS

In the treatment of all gonococcus infections, in whatever clinical form general or localized including gonorrhea they may appear the essential feature is the eradication as early and as completely as possible of the infecting organism the gonococcus To this end an antibacterial effective on the gonococcus is to be used

Penicillin is the most effective of these and is strongly advised for the treatment of all gonococcic infections The following dosages of penicillin are satisfactory and are suggested for use For *urethritis* a dose totaling 200 000 units of penicillin dissolved in physiological salt solution with 80 000 units in the first dose followed at 3 hour intervals by 3 doses of 40 000 units each all given intramuscularly or intravenously is recommended Penicillin as procaine penicillin in aqueous suspension given intramuscularly, may be used instead of the aqueous solution a dose of 300 000 units being injected and repeated in 12 to 24 hours More units of penicillin and longer periods of treatment may sometimes be required to eradicate the gonococci from the urethral discharge Until this has been done the treatment used has been unsatisfactory and should be continued or repeated

Other antibiotics besides penicillin are effective against the gonococcus and probably will come to play an increasing role in the diseases of gonococcal etiology They are aureomycin chloramphenicol and terramycin and are given by mouth in a total dosage of 2 gm to 3 gm each 24 hours subdivided into individual doses given every 3 to 6 hours

For gonococcal *arthritis* more units of penicillin over a longer period of time are usually needed for cure Recent recommendations for dosage made by the editorial committee of the American Rheumatism Association are 25 000 to 30 000 units every 3 hours for from 7 to 10 days If there is no improvement in 3 or 4 days intra articular injections of at least 10 000 to 20 000 units once daily are given when possible

For gonococcus *endocarditis* still larger daily dosage of penicillin 500 000 to 1 000 000 units repeated over many days as described for the treatment of Subacute Bacterial Endocarditis will almost certainly be required Vulvovaginitis in young girls should be treated under the direction of a gynecologist Strict isolation may be impractical but it is essential that such patients remain away from school and other public places while infectious Great care must be taken to instruct the child so that infections elsewhere will be avoided especially in the eye and rectum Penicillin in large doses is effective and should be started

promptly in a dose of 20 000 to 30 000 units intramuscularly every 2 hours A single intramuscular injection of 300,000 units as procaine penicillin in aqueous suspension or penicillin in oil and beeswax also is effective Oral penicillin 50,000 units every 2 hours for 10 doses, may be given also, especially to younger girls Occasionally, in the highly resistant case, it may be necessary to use sulfadiazine or a combination of penicillin and sulfadiazine with an estrogenic substance Suppositories containing 0 05 to 0 1 mg of stilbesterol inserted into the vagina daily for 3 weeks or 0 1 mg of stilbestrol a day orally may be of assistance This treatment may be repeated once but prolonged administration leads to undesirable sex characteristic changes The preceding suggestions for dosage may be applied in any other of the clinical forms of gonococcus infection if they are regarded as guides to, rather than fixed formulas of treatment

In some of the gonococcal infections such as *arthritis*, *synovitis*, et cetera splints or casts are often needed to minimize painful movements In many of the gonococcic infections a localized inflammatory process develops which may require either tapping or surgical drainage, and possibly excision followed by injection of a solution containing 20,000 to 50 000 units of penicillin

In gonococcal *meningitis* penicillin needs to be given intrathecally, in doses of 15 000 to 20 000 units once or twice a day in addition to intra muscular or intravenous injections

At present a *sulfonamide* is recommended for use in the treatment of gonococcus infections only when penicillin therapy is not available or when the infecting organism has proved very resistant to penicillin, in which event both sulfadiazine and penicillin should be given The plan of dosage of sulfadiazine should be that described in Chapter I

The important thing is not to consider any treatment of gonococcus infections as satisfactorily completed until the presence of the gonococcus can no longer be detected by microscopic and cultural techniques Repeated examinations should be spaced at increasing intervals of time beginning with one week Remember too that as a general considera tion the most important gonococcic infection to treat until the infecting organism is completely and permanently eradicated is the primary infection in the male or female genito urinary tract because this is causa tive of the many clinical forms of gonococcal infection In the male, microscopic examination and culture should show the absence of gonococci from the urethral fluid obtained after intrarectal massage of the prostate In the female similarly proved absence of gonococci from

urethral and cervical secretions before and after menstruation for three successive months should be considered the only satisfactory evidence of cure

It is to be remembered that the patient with a gonococcus infection, especially one of the genito urinary tract very often has a simultaneous infection with syphilis When penicillin is used in treating gonococcal infection, the usual quick response of syphilis to penicillin therapy can easily mask clinical evidences of syphilis and its presence may escape recognition unless careful diagnostic procedures are followed Sero logical tests for syphilis should be repeated monthly for 4 to 6 months after eradication of gonococci and then at 6 month and yearly intervals for more years If in addition to the gonococcic infection syphilitic infection is present the best treatment for the latter must of course be given (see under Syphilis p 233) as well as the measures being used for the gonococcic infection

General measures as described in Chapter I should be applied in the treatment of gonococcic infections as well as the specific antibiotic and antibacterial therapy just mentioned Everything coming in possible contact with discharges from the patient including gauze or other dressings that probably contain gonococci must be boiled chemically sterilized or destroyed promptly Particular care must be taken to keep the gonococci from infecting the eyes of the patient and of any person coming in contact with him if there has been a possibility of infection or if there is any suggestion of conjunctivitis penicillin in normal saline solution containing 500 units of penicillin per cc should be instilled into the conjunctival sac at once

If, despite these precautions *gonococcal ophthalmia* develops treat ment should be prompt and thorough preferably under the direction of a skilled ophthalmologist For this atropine sulfate 1 per cent should be promptly instilled into the eye and repeated as needed to keep the iris at maximum dilatation A saline solution of penicillin containing 500 units per cc should be instilled into the eye every 5 minutes for 1 to 2 hours or until there is no further discharge then at half hour to 1 hour intervals for 12 to 24 hours This should be continued at 2 hour intervals for 24 hours or until the conjunctiva has a normal appearance Intramuscular penicillin in a dose of 50 000 units every 3 hours or procaine penicillin in aqueous suspension 300 000 units at 12 hour intervals should also be given to bring about a rapid remission

Prophylaxis against gonococcus infections is very important from both the personal and the public health point of view Gonococcic infections

may involve locally almost any part of the body or may take on a general septicemic form All of these can be considered as secondary to, or as complications of gonococcic disease of the genito urinary tract, especially of gonococcic urethritis or gonorrhea Their prevention then depends on the prevention or the very speedy cure of gonococcic urethritis and gonococcic infection of the urethral adnexa Every patient with such gonococcic infection should be isolated at once and thoroughly treated, contacts should be searched for and similarly managed All infected persons must be reported as required by local boards of health or state departments of public health The physician must familiarize himself with such rules and regulations and should encourage and participate in education about the dangers of gonorrhea, in doing these things he is playing an important role in public health

Chancroidal Infections

Chancroidal lesions produced by the *Streptobacillus of Ducrey,* on the penis vulva introitus cervix and other mucous membrane areas respond readily to cleanliness and to aureomycin applied locally and systemically The ulcerated area should be washed thoroughly with soap and water at least twice a day and a 3 per cent ointment of aureomycin applied In cases of deep or extensive ulceration healing is hastened by the oral administration of aureomycin 1 to 2 gm a day, for 1 to 2 weeks or until complete healing has taken place Sulfadiazine in the usual dosage is also highly effective and the cost of treatment is much less Penicillin does not give satisfactory results Local application of 2 per cent allantoin ointment hastens healing in a large ulcerated area Lesions should heal without scar formation in from *5 to 10 days*

Sexual intercourse is forbidden until healing of chancroidal lesions is complete Patients should be repeatedly checked for syphilis in the manner recommended under the discussion of Gonorrhea, since syphilis may be masked by antibiotic treatment

Whooping Cough

Once the infection is established treatment should consist of bed rest during the acute phase especially if the paroxysms are frequent or severe, or if fever is present Expert nursing care is essential and will do much to prevent some of the unpleasant complications Nutrition should be maintained at a high level and care should be taken to repeat feedings

when paroxysms lead to vomiting, usually a lapse of 15 minutes is sufficient before refeeding It is better to give nourishment in small quantities at frequent intervals than to give a few large feedings The patient s room should be well ventilated free of irritating dust and smoke and the temperature should not fluctuate widely The humidity should be kept high An abdominal binder will lend support and prove comforting

Aureomycin is an effective antibiotic, especially if it is begun in the very early stages of the disease Dosage should be 60 mg per kilogram of body weight every 4 hours subdivided into 4 to 6 oral doses

Terramycin given in the same dosage by mouth is effective too as are oral doses of the same quantity of chloramphenicol As there is now a range of antibiotics with which to treat pertussis it is probable that an antibiotic will replace much of the treatment previously advised for this disease Injections of pertussis vaccine 1 0 cc repeated in 2 weeks may help those immunized by previous vaccination The ideal drug for the treatment of pertussis has not yet been developed

Patients exhibiting dyspnea cyanosis or convulsions are often relieved by oxygen combined with enough carbon dioxide to avoid the drying and anti-expectorant effects of the oxygen alone Accumulations of mucus, causing strangling or blockage of the respiratory tree should be removed by aspiration Human plasma 0 to 40 cc intramuscularly is of assistance Antipertussis serum (rabbit) is better and a dose of 5 to 10 cc is recommended for infants In older children if no improvement is shown in 48 hours another dose of 10 cc should be given Concentrated human hyperimmune serum (Hypertussis) is even better and may be given in a dose of 2 5 to 5 0 cc intramuscularly For infants under one year of age, 2 5 cc is recommended initially to be repeated in 24 to 48 hours as necessary

If anemia is present small whole blood transfusions are of value also and may prove most helpful

Convulsions may be relieved by lumbar puncture or controlled by subcutaneous injections of sodium phenobarbital the dosage depending on the age of the patient and the severity of the attack and ranging from 0 03 to 0 06 gm for infants from 6 months to a year and from 0 06 to 0 2 gm for children from 2 to 3 years of age Adults may receive from 0 12 to 0 3 gm Care must be taken to avoid overdosage Magnesium sulphate 45 mg per kilogram of body weight given intramuscularly may prove helpful if convulsions persist Finally in severe cases the rectal installation of 4 to 8 cc of ether dissolved in olive oil is a safe sedative and is usually effective

In the absence of convulsions or severe paroxysms, sedation should be held to a minimum and avoided whenever possible Certainly sedatives should not be used to the extent that they cause abdominal distention When mild sedation is indicated chloral hydrate, 0 3 to 0 6 gm dissolved in olive oil or water and given by rectum is useful Sodium pheno barbital 0 03 to 0 1 gm dissolved in tap water and given by rectum, suffices for infants while young children respond well to doses of 30 mg to 0 2 gm Adults may be given 0 2 to 0 3 gm

If severe irritating non productive cough becomes a problem, codeine phosphate in a dose of 2 5 to 10 mg is effective in infants and young children Older children and adults may be given 15 to 30 mg Dihydrocodeinone (Hycodan) bitartrate 1 to 5 mg for children under 2 years, 2 to 8 mg for children over 2 years, and 5 to 15 mg for adults repeated 3 or 4 times in 24 hours preferably after meals is very effective and is without many of the side reactions of codeine such as nausea and con stipation Steam inhalations to which benzoin or eucalyptus has been added are soothing and may give considerable relief For intractable cough one teaspoonful doses of a mixture of equal parts of a syrup of glyceryl guaiacolate plus desoxyephedrine hydrochloride (Robitussin) and the syrup of Hycodan are very effective

After convalescence has begun the patient should be watched carefully since bronchopneumonia and other complicating conditions are likely to appear Plenty of fresh air sunshine nutritious food, rest and well regulated activities will do much to bring about final complete recovery

Prophylaxis Whooping cough should be prevented as far as possible by avoiding exposure and by active immunization with a vaccine made from a highly antigenic strain of organisms For the latter 1 cc of a vaccine prepared from a smooth (phase 1) recently isolated culture of *Hemophilus pertussis* containing 15 billion organisms should be given subcutaneously After 1 month a second dose of 2 cc of this vaccine should be given followed in another month by a dose of 3 cc For younger children the 3 cc dose may be reduced to 2 cc, 1 cc being given in each arm Some merit is claimed for immunizing pregnant women to transmit the immunity through the placenta to the unborn child Every effort should be made to prevent the disease in the infant under 1 year of age Vaccination although known to be less effective if given to a child under the age of 8 months is recommended by some authorities to be started at the third or fourth month of age in order to establish some immunity within the first year For this purpose three

SUPPLEMENTARY INDEX 1

5 McMORROW, K J and TOP F H 'Treatment of Hemophilus Influenzae B Meningitis 67 Cases, *J Pediat*, 1950, v, p 452

Gonococcus Infections

1 BEINFIELD M S WRIGHT L T DELUCA, F R et al Comparative Study of Oral Terramycin and Aureomycin Therapy of Gonorrhea in Males *N Y State Jour Med*, 1951, LI, p 1054
2 CHEN C H DIENST R B and GREENBLATT, R B The Treatment of Gonorrhea with Chloramphenicol *South, Med Jour*, 1949 XLII p 986
3 SCOTT M J Antibiotic Drugs in Veneral Disease Therapy," *U S Armed Forces Med Jour* 1951 1 p 1017

Chancroidal Infections

1 LONG P H CHANDLER C A BLISS E A MORTON S and SCHOENBACH E B Use of Antibiotics *Jour Amer Med Assoc* 1949 CXLI, p 315
2 WILCOX R R Streptomycin in Soft Sore Observations on Clinical and Experimental Infections *Lancet*, 1950 1 p 396
3 ZHEUTLIN H E C and ROBINSON R C V Aureomycin Therapy in Chancroid *Am J Syph* 1950 XXXIV, p 71

Whooping Cough

1 BOOHER C E FARRELL J B and WEST E J Pertussis Clinical Comparison of Newer Antibiotics *J Pediat*, 1951 XXXVII, p 411

subcutaneous injections of 0 2 0 3 and 0 5 cc increased to three 0 5 cc doses for older patients of an alum preparation totaling 40 billion bacilli per cc are recommended

The nodule formation and reactions to this vaccine are obviated somewhat by warming the vaccine shaking it thoroughly and making a deep subcutaneous injection and then massaging the injection site Such procedures may protect and certainly do alter the course of the disease Passive immunization for exposed young infants can be given by intramuscular injections of o to 40 cc of adult plasma 10 to 30 cc of hyperimmune human serum or 5 to 10 cc of antipertussis serum prepared from the rabbit

BIBLIOGRAPHY

Cerebrospinal Fever

1 HOYNE, A L Modern Treatment of Meningitis *Texas State Jour Med* 1950 XLVI p 33

2 LONG P H Clinical Use of Antibiotics *Med Clin No Amer* March 1950 p 307

3 NELSON J and GOLDSTEIN N Nature of Waterhouse Friderichsen Syndrome Report of Case with Successful Treatment with Cortisone *Jour Amer Med Assoc* 1951 CXLVI p 1193

4 TORSTENSON T Report on Combined Sulfonamides Penicillin Treatment of Acute Purulent Meningitis and Follow up Study *Acta Paediat* 1949 XXXVII p 377

Influenzal Meningitis

1 APPLEBAUM E and NELSON J Streptomycin in the Treatment of Influenzal Meningitis *Jour Amer Med Assoc* 1950 CXLIII p 715

2 BLOOR B M GRANT R S and TABRIS J A Sequelae of Meningitis Due to Hemophilus Influenzae *Jour Amer Med Assoc* 1950 CXLII p 241

3 CARABELLE, R W MITCHELL D D and SALMON G W Influenzal Meningitis Treated with Chloromycetin *J Pediat*, 1950 XXXVII p 37

4 DRAKE M E BRADLEY J E IMBURG J McCRUMB F R Jr and WOODWARD T E Aureomycin in the Treatment of Influenzal Meningitis *Jour Amer Med Assoc* 1950 CXLII p 463

must be boiled or otherwise sterilized promptly after use Bed linen should be sterilized by steam or soaked for not less than 2 hours in 1 2000 bichloride of mercury before being sent to the laundry Bedpans and urinals should be sterilized by boiling by live steam or by chemicals after use certainly before use by others Feces and urine before disposal should be treated with live steam or with chemicals To the urine should be added equal parts of 1 to 20 carbolic acid or one-fifth volume of 1 1000 bichloride of mercury and the mixture allowed to stand for 3 hours to the feces should be added 3 parts of either 1 to 20 carbolic acid or freshly prepared quick lime or equal parts of 10 per cent farmaldehyde these mixtures should stand for at least 3 hours Sputum should be collected on gauze or tissue and burned

If it is necessary to place typhoid patients in a room where there are non typhoid patients this can be done with safety provided all who come in contact with the typhoid wear protective gowns and head coverings wash their hands with soap and warm water and then soak them in an antiseptic solution Everything used by or in contact with, the typhoid patient must be sterilized promptly as described in the preceding paragraph

Treatment with Antibiotics

Chloramphenicol given by mouth is such an effective antibacterial against typhoid bacilli that it should be given to every patient as soon as the diagnosis of typhoid fever has been made The initial dose by mouth should be 60 mg per kilogram of patient s body weight followed by 0 25 gm given every 2 hours around the clock until the fever falls well toward normal and then every 3 or 4 hours for 14 days

Another effective procedure is to give an initial dose by mouth of 3 0 to 4 0 gm followed by 1 5 gm doses every 12 hours so long as fever persists, then 1 0 gm twice a day for 7 days after which the doses should be reduced to 1 0 gm daily until the end of the fourteenth day of antibiotic therapy

Terramycin may also be of value and should be tried if chloramphenicol cannot be used A dose of 100 to 00 mg per kilogram of body weight given in 6 divided doses is recommended The larger dose should be given in severe cases The antibiotic should be continued for 3 weeks

During the period of antibiotic treatment the general measures for infectious diseases as given in Chapter I including the diet there

CHAPTER VII

TYPHOID, COLON, AND BRUCELLA GROUP OF DISEASES

Typhoid Fever

Typhoid fever is a systemic infectious disease and not merely an ulcerative disease of the intestine as was once believed This being true medicaments that act directly on the intestinal lesions such as intestinal antiseptics are not effective An antibacterial effective on the causative bacilli has been needed in treatment but until recently none had been developed Now however it seems that an effective antibacterial for typhoid bacilli has been found in chloramphenicol and possibly in terramycin As this has completely changed the plan of treatment advisable for patients with typhoid fever the treatment will be discussed in two main parts (1) treatment with antibiotics for patients in whom an antibacterial is promptly effective and (2) treatment without an antibiotic for patients in whom it has not been satisfactorily effective or for times when this antibacterial is not available These will be preceded by directions for isolation and followed by directions for treating complications important with either plan of treatment

Isolation

Whenever possible the typhoid patient should be put in a single room or in a room where there are only patients with typhoid All who come in contact with a typhoid patient should wear gowns and head coverings Before being sent to the laundry this clothing should be kept separately until sterilized either in a steam sterilizer or by boiling All who come in contact with the typhoid patient should after leaving wash their hands thoroughly with soap and warm water and then soak them for not less than 3 minutes in 1 1000 tincture of benzalkonium (Zephiran) chloride or 1 10 000 bichloride of mercury Everything used by the patient

pleasant dentifrice on a soft tooth brush and cleaning between the teeth with dental floss The mouth should be cleaned with Alkaline Aromatic Solution — N F or compound Sodium Borate Solution (Dobell's Solution) every 3 or 4 hours If the mouth is dry a slippery elm lozenge can be sucked or a small amount of dilute glycerine containing a few drops of lemon juice put into the mouth, either will decrease the dryness of the mouth mucosal surfaces and make the mouth feel better

Diet For the typhoid patient the diet must be composed of liquids, soft solids pureed vegetables, and scraped meat and fish Food items should be changed from day to day to avoid monotony Sick typhoid patients usually cannot manage foods requiring more than a very little chewing The diet should contain 3000 to 4000 or even more calories per day as the ideal to strive for To reach this amount usually requires great diligence and persuasiveness on the part of the nurse who feeds the patient All typhoid patients more than mildly ill require feeding by the nurse

The following food items are suggested as filling the requirements of a diet suitable for the patient with typhoid milk cream, eggs, scraped meat and fish cooked fresh fruit and canned fruit both without skins or seeds fruit juices boiled rice mashed potatoes, cooked cereals, bread, macaroni spaghetti pureed vegetables butter custards junket, jellies, ice creams various flavored milk drinks coffee tea postum, or Sanka with cream and sugar The daily diet should include 2 gm of protein per kilogram of body weight and 10 gm of salt With these food articles, if taken in variety sufficient vitamins will be present Usually feedings are given every 2 hours through the day and during waking hours at night The more stuporous patients may have to be given a diet composed mainly of fluid elements more alert patients can be given the other items a few patients can be given food that needs to be chewed, such as dry toast

A basic diet for 3 meals breakfast dinner and supper given at 8 a m, 12 noon and 6 p m — which will yield on the average 3000 calories — can be composed as shown in the following samples Additional calories, as needed can be given at 10 a m 4 and 8 p m in the form of various drinks, sweetened with sugar or glucose the latter making them less sweet and so preferred by some patients Lactose may be used to flavor the drink it is not so sweet and it is not fermented by the typhoid bacilli — which may or may not be an advantage in its favor

A sample basic diet for typhoid fever follows

described will suffice Isolation however, as already described under that heading should be carried out meticulously and the patient kept under very careful observation to detect the onset of complications which may develop even during or subsequent to a successful course of treatment with chloramphenicol or terramycin

Treatment without Antibiotics

If treatment with antibiotics does not bring about a normal temperature within 5 days or if they are not available or are ineffective the regime formerly advised for all typhoid patients should be commenced This will be described in the following paragraphs with isolation carried out as already outlined

Nursing Care Skilled nursing is necessary to the proper care of *typhoid patients not receiving or found resistant to antibiotics* Among the duties of the nurse are making the patient comfortable in bed at all times assisting in oral hygiene feeding the prescribed diet maintaining the needed fluid intake, giving bed baths applying hydrotherapy and caring for the skin so as to prevent bed sores The nurse should assist in the use of urinal and bedpan and then meticulously cleanse and dry the perineal and periurethral skin Measures should be taken to minimize the incidence of phlebothrombosis and the nurse should be on the alert to recognize the beginnings of complications keep accurate record of food and fluid intake temperature pulse rate respiration rate, bowel movements and urine amount maintain patient morale and carry out measures to prevent spread of typhoid to others

Typhoid patients should have cleansing bed baths twice daily followed by complete drying of the skin and subsequent powdering with any good toilet powder preferably one pleasantly perfumed A back rub with dilute alcohol helps to keep the skin in good condition Whenever defecation or urination occurs the nurse must make certain of complete cleansing of adjacent parts their drying and then their powdering If signs of pressure appear over places where bones are close to the surface this skin should be kept particularly clean and dry and be protected from pressure by frequently shifting the patient s position and by the use of protective rubber or gauze rings — doughnuts as they are called All of these nursing procedures are particularly important to the patient delirious or in stupor

Oral care should include frequent brushing of the teeth with a

Frequently with such a diet there is moderate constipation If so, a bland enema should be given every other day, cathartics should not be used If distention develops carbohydrate elements of the diet should be reduced Persisting distention should be treated as described below If a slight diarrhea is present, the diet should be reduced temporarily, if diarrhea becomes severe it should be corrected

Fluid Intake Dehydration should be prevented by a fluid intake sufficient to cause a minimal 24-hour urine output of 1500 cc To obtain this in addition to the fluid in the feedings every 2 hours, the patient should be given a measured amount of water during the intervening hours of the day and every 2 hours during the night, if not asleep Most typhoid patients while febrile need 4000 to 5000 cc of fluid each 24 hours Besides preventing dehydration the drinking of water is an aid in oral hygiene and reduces that dry feeling in the mouth which is often a source of discomfort to the typhoid patient

If dehydration is not corrected by the preceding methods which is unusual normal saline with 5 per cent glucose warmed to body temperature should be given slowly intravenously to make up any deficit

Hydrotherapy Sponging and wet packs are frequently indicated and are extremely useful in the care of the patient with typhoid fever For sponging the water may be tepid or cold depending in part upon the height of the fever and in part on the preference of the patient The greatest care should be taken to sponge the abdomen very lightly so that mechanical trauma does not result Packs are most useful when there are pronounced symptoms of the central nervous system, particularly delerium To give a wet pack wrap the naked patient in a sheet wrung out of water at 60 to 65°F then sprinkle cold water over him at frequent intervals

Medicinal Treatment

Drugs, except a specifically acting antibiotic have little part in the treatment of typhoid fever Antiphlogistic drugs seem undesirable Cathartics should not be given An occasional patient needs sedation as already described for other infectious diseases

Mandelamine With the use of chloramphenicol it is possible that typhoid bacilluria will not occur If it does it will be advisable to give methenamine mandalate (Mandelamine) by mouth Beginning with the third week of the disease give 1 to 3 gm of the drug daily This should be continued so long as urine cultures remain positive for typhoid bacilli

Basic Diet for Non-stuporous Patients with Typhoid

3000 + Calories

Breakfast	*Calories*
Strained orange juice with 1 tsp sugar	68
Egg 1 soft-cooked	78
White toast 1 slice	84
Butter sq 10 gm	72
Cooked cereal 120 cc	11
(rice cream of wheat or strained oatmeal) with	
60 cc cream 40 %	468
Tea or coffee with 40 % cream and sugar	232
	1114
Noon meal	
Creamed chicken or fish or scraped beef ball	165
Potato baked mashed or creamed	84
Pureed green vegetable	28
White bread 1 slice	84
Butter 2 sq 10 gm	7
Soft dessert (custard ice cream sherbet plain blanc mange jellies whips bavarian cream tapioca or rice pudding sponge cake may be flavored or served with fruit juice or pureed fruit)	154
Milk 1 glass	152
Cocoa (milk 120 cc 40 % cream 60 cc cocoa and sugar 1 tsp	341
	1080
Supper	
Creamed vegetable or chicken soup	00
Creamed toast rice or macaroni	170
Pureed vegetable	28
Strained apple sauce or other pureed cooked fruit with sugar	80
Cream cheese	131
White crackers 2	53
Butter 10 gm	72
Cocoa	341
	1075

Total 3269 calories

Note—These three meals are to be supplemented when the patient's condition indicates that more calories are needed by between meal feedings of drinks made from milk cream malted milk and eggs or fruit juices or cereals and gruels with plain milk or cream according to patient's taste so that total calories may reach 5000 or more Any of these should be sweetened to taste with sugar (sucrose) or if patient finds them too sweet lactose may be substituted for sugar

Water is to be given in addition so that patient receives in all the amount of fluid ordered by the physician

when bleeding occurs the physician must search carefully for signs of perforation

Intestinal Perforation This is indicated by quickly developing localized abdominal pain tenderness and/or spasm, a rising leucocyte count and possibly signs of free fluid or gas in the abdominal cavity, the latter demonstrable by x-ray If perforation develops, it should be treated by immediate surgical opening of the abdomen search for the site of perforation, and its closure by suture It is better if in doubt, to carry out an abdominal exploration rathen than to await more convincing signs, delay in exploration in all probability will make certain the development of acute, probably fatal peritonitis Antibiotic therapy is advisable if perforation is discovered particularly when peritonitis is found In these patients streptococci are the organisms most serious in their results, they are susceptible to penicillin, which should be given systemically and locally in large dosage As colon bacilli also will be present, the use of streptomycin with penicillin is recommended Chloramphenicol, aureomycin and terramycin are also useful in cases of perforation However these agents may interfere with the action of penicillin — which streptomycin does not do If one of these antibiotics is being given, it should not be discontinued Perforation calls for prompt consultation with a skilled surgeon who should take over so far as the immediate treatment of the patient is concerned Some patients with perforation have been treated successfully with only antibiotics and no surgery

Abdominal Distension (Tympanites and Abdominal Discomfort) With diet and fluid intake and cleansing enemas as already described, marked abdominal distension or tympanites is unusual With the use of chloramphenicol it may become only a historical fear in typhoid fever If it does develop to a marked degree however the possibility of intestinal hemorrhage or perforation should be thought of and ruled out If these are not believed to be present and distension is marked a rectal tube should be passed and left in place often this relieves the distention If not, a tube (Abbott-Miller) should be passed through the stomach into the small intestine and left in place this will relieve small intestine distention Both tubes are safe since usually typhoid ulcerations are beyond the point of reach of each tube

Medical treatment of abdominal distention should be used too along with reduction in the carbohydrate moiety of the diet even though this, as a rule, has little responsibility in producing the distention Neostigmine (Prostigmine) methyl sulfate should be given intramuscularly in a dose of 0 5 mg (1 cc of a 1 2000 solution) every 30 to 60 minutes

Antibacterials even though promptly effective may not do more than decrease the frequency of the following complications although there is now some evidence that prolonged dosage with chloramphenicol will do away with them Consequently they must be carefully watched for and treated promptly as in the years before the development of effective antibacterial therapy

Intestinal Hemorrhage This very important special symptom or complication occurs when the base of an intestinal ulcer sloughs away to expose an artery not as yet obstructed by thrombus It is a part of the pathological process and remains in some measure if not entirely unrelated to treatment or lack of treatment It cannot be anticipated since small bleedings enough to cause a positive guaiac or benzidine reaction in the stool often occur with no subsequent gross hemorrhage and gross hemorrhage may not be preceded by a small bleeding to give positive results from these tests Hemorrhage is obvious when blood appears in the stool If there has been a large hemorrhage there are such symptoms as faintness with pallor or actual collapse increased pulse rate fall in temperature sometimes abdominal distension and possibly abdominal pain If these occur to suggest intestinal hemorrhage treatment should be begun at once Food should be stopped for 4 hours The patient should be urged to lie quietly flat on his back and should be disturbed as little as possible If he is restless cold compresses may be placed lightly on the abdomen morphine sulfate should be given in repeated doses of 6 to 8 mg until restlessness is controlled and peristalsis is lessened Many clinicians who have treated great numbers of patients with typhoid fever have used morphine in this way for years with confidence in its effectiveness

The bleeding patient should make no effort to move his bowels If the urge comes the patient should be helped gently onto a bedpan many advise against using the bedpan and allow the patient to empty his bowels on the draw sheet what is passed usually is almost entirely blood sometimes bright red and unclotted

Blood transfusion should be given only when the patient s condition is one of evident collapse For most patients immediate transfusion of blood is not needed and often they are better off without it After the bleeding seemingly has ceased if there is as occasionally happens evidence of anemia transfusions of 250 to 300 cc of whole blood are advisable and should be repeated until the anemia is corrected Since intestinal bleeding may be precursor to or accompanied by perforation

Circulatory Failure The type of circulatory failure manifest in typhoid fever in past years was either that of peripheral vascular collapse associated with blood loss from intestinal hemorrhage or that of the acute circulatory failure of infectious disease The former is best treated by properly spaced transfusions of the needed amount of whole blood, the latter type is to be treated as described under Pneumonia In older patients with typhoid fever, organic cardiac disease may exist and, with evidence of myocardial insufficiency, fibrillation or auricular flutter, digitalis and other drugs of this group are indicated Such drugs as strychnine, coramine and camphor derivatives are of temporary benefit, if of use at all, in the circulatory failure of typhoid

Convalescence

The convalescent period should be a prolonged one for the patient whose febrile period has been long as was usual before introduction of the use of chloramphenicol, great judgment must be used, with consideration given to the age of the patient the severity of the illness, and its duration The diet may be increased gradually in variety so as to approach an eventually normal diet The patient should remain flat in bed for a week after a normal temperature has been attained, then gradually be allowed increased periods of sitting up in bed, followed by slowly increasing periods out of bed and finally walking, et cetera, as discussed in Chapter 1 During this period any rise in fever or increase in pulse rate is a sign that too rapid progress is being made in the convalescence and that there should be more rest If the febrile period is short as seems probable with the use of chloramphenicol this period of convalescence can be greatly shortened

Carriers Most important during convalescence is to attempt to determine whether or not the individual will be a carrier of typhoid bacilli It is a rule in most communities that the patient recovering from typhoid fever is not to be discharged from the hospital until 3 consecutive stool cultures have been negative for this organism Likewise, 3 consecutive urine cultures should also be negative If an individual is found to be a carrier chloramphenicol should be given as described for treatment Much continued observation is needed to determine the effectiveness of antibacterials in the carriers of typhoid bacilli but from data now available they are not very effective If the organisms are found to be harbored in the gall bladder and biliary system, a cholecystectomy should

until distention is relieved or slight toxicity such as salivation nausea, or flushing of the skin appears Neostigmine bromide also can be used by mouth in doses of 15 mg If this treatment is unsuccessful, pituitary extract (Pitressin), 1 cc of a 1 1000 solution subcutaneously should be tried except in arteriosclerotic cardiac or elderly patients who may get an undesirable coronary constricting effect from it

Warm compresses should be applied over the abdomen Some still prefer to use the turpentine stupe applying it very hot over the abdomen which has been well greased with petrolatum jelly This stupe is made by pouring boiling water to which has been added turpentine 1 tea spoonful to the quart over a turkish towel and wringing the towel out quickly by twisting it in a second dry turkish towel The stupe should be applied while very hot when it cools another hot stupe should replace it and this should be repeated as long as good effects result

When distention develops fecal impaction may be the cause con sequently rectal examination should be made If impacted feces are found they should be removed manually after being softened by a preceding oil enema Impaction of feces is unusual in the early days of typhoid fever

If distention is only slight, reduction in carbohydrates in the diet a cleansing enema a rectal tube and warm compresses on the abdomen usually suffice and the other measures just described are not needed

Some advise giving an evening dose of a tablespoonful of castor oil as a corrective of abdominal distention Experience shows that castor oil is entirely safe and does not cause intestinal hemorrhage or perforation

Abdominal discomfort often accompanies the distention but actual pain is not present or is only slight If there is sharp pain perforation is probable and its possible presence should be considered carefully with all appropriate diagnostic methods Morphine should not be used in treating abdominal discomfort or pain for it may mask signs of per foration by making the patient unaware of localized abdominal pain

Cholecystitis When this symptom develops it usually subsides spontaneously under symptomatic therapy With the use of chloramphenicol typhoidal cholecystitis is unlikely If acute cholecystitis does develop in these circumstances it is probably streptococcal and should be treated as described for Cholecystitis If the symptoms of cholecystitis are severe progressive and unresponsive to the treatment just advised immediate operation is indicated If the symptoms subside removal of the gall bladder should be considered for the incidence of cholelithiasis subsequent to typhoidal cholecystitis is high

Occasionally a reaction follows inoculation, such as fever, headaches, arthralgia chilliness, abdominal pain, nausea, vomiting or diarrhea The treatment consists of rest, a light diet no alcoholic drinks symptomatic salicylates, and, possibly, the use of one of the antihistaminic agents

SALMONELLOSIS

Treatment of salmonellosis an inclusive term for infections with various members of the Salmonella genus of bacteria including what was formerly called the paratyphoid group of organisms may be divided into three phases (1) general measures as applicable to all infectious diseases (see Chapter I), (2) the use of specific antibiotics, and (3) local treatment There are a great many bacteria in the salmonella group differing more or less from each other in cultural and immunological characteristics and they cause a variety of clinical syndromes which may be subdivided into four groups (1) typhoid like or paratyphoid, (2) septicemia (3) gastro enteritis and (4) localized infections such as pharyngitis, otitis media empyema pyelitis pyelonephritis arthritis cholecystitis, appendicitis meningitis and abscesses in various organs and tissues singly or in various combinations Carriers exist with considerable frequency

General measures for patients with salmonella infections requiring long continued fever treatment are for the most part those described for typhoid fever including the use of chloramphenicol In addition to these general measures patients with the gastro enteric form should have special attention in regard to diarrhea a simple liquid diet with tincture of opium camphorated tincture of opium (paregoric) or aluminum hydroxide compounds sufficient fluid by mouth or parenterally to prevent dehydration and isolation with sterilization or other sanitary disposal of stools are recommended Some advise giving castor oil daily for a few days in tablespoon doses The gastro enteric form is often of the nature of a food poisoning raising the problem of detection of carriers and prevention of food contamination besides those of isolation and sanitary disposal of the stools of active cases and carriers

Antibiotics have not been very satisfactory for the salmonella group Some organisms of the group are susceptible to streptomycin, while others are quite resistant to it Some of the group are fairly susceptible to a sulfonamide such as sulfadiazine or when in the intestinal tract, to the very slightly absorbable sulfonamides sulfasuccidine and sul-

be considered but it has been effective in eliminating the carrier state in only about half the cases in which it has been done Most important is to recognize the fact that the individual is a carrier, to enforce utmost cleanliness in personal hygiene and not to allow the individual to handle or prepare food in any manner In the case of a typhoid carrier the handling of the situation should be turned over to the local board of health

Prophylaxis

The prophylaxis of typhoid fever includes (1) the early recognition and prompt treatment of all cases with this disease and ( ) the isolation of the patient including every effort to kill all typhoid organisms on or in the excretions of the patient Both factors include proper isolation of the patient as already discussed with particular emphasis on screening against flies and the use of fly repellants and exterminators and decontamination of all articles and persons coming into contact with the patient This includes chiefly disinfection of all excreta utensils and linens and proper decontamination precautions by all attendants including the physician

Urine feces and sputum should be treated as described in the section on Isolation in Chapter I

Meticulous cleanliness must be carried out by the nurse and all attendants A rubber apron and rubber gloves should be used by anyone handling the patient then promptly washed with bichloride of mercury or boiled Preventive inoculation should be given to all those coming into contact with the patient

Inoculations These have proved beyond any question to be of inestimable value with protection afforded for 3 years or longer by booster doses The most effective inoculation and the one least causative of reactions is triple typhoid vaccine (containing typhoid and paratyphoid organisms) given intracutaneously The dose is 0 1 cc 0 15 cc and 0 2 cc at weekly intervals Protection may be enhanced by giving 0 1 cc each year

The older method very effective but producing more frequent local and systemic reactions consists of the use of the same vaccine given subcutaneously 0 5 cc 1 0 cc and 1 0 cc at weekly intervals then 0 5 cc each year for added protection

Vaccination by the oral administration of killed typhoid organisms after the principles of Besredka is sporadically effective with results not consistent enough to warrant recommending it Its use is not advised

Members of the colon bacillus group are very similar to those of the salmonella group in susceptibility to antibiotics, i e some are susceptible to a sulfonamide some to streptomycin some to chloramphenicol, and none to penicillin Tests of susceptibility should be used to determine the selection and dosage of the antibacterial most likely to be therapeutically effective in the individual patient If the patient is severely ill, the antibiotic that has proved effective against the infecting type of colon bacillus should be given

Bacillary Dysentery Shigella Enteritis

Treatment of bacillary dysentery should begin with prompt and complete bed rest The patient should be kept in bed until the acute episode is over and the content and number of stools approach normal The isolation precautions described for typhoid must be enforced

Diet With acutely nauseated patients with considerable abdominal cramping, it is best to withhold food for 24 hours and then start a fluid diet consisting of rice or barley water clear broths and tea served warm and at frequent intervals As improvement occurs the diet should be increased by the addition of strained gruels soft-boiled eggs, toast, butter custards, puddings well cooked cereals, and still later scraped broiled chicken Fluids sufficient to maintain a daily urinary output of at least 1500 cc should be given either by mouth or parenterally

Intestinal cramps are best managed by giving atropine sulfate, 1 0 mg subcutaneously repeated in 6 to 8 hours if necessary, or homatropine methyl bromide 2 5 to 5 mg every 4 hours If there is considerable pain meperidine (Demerol) hydrochloride 0 1 gm or methadone hydrochloride 5 to 10 mg given hypodermically every 3 or 4 hours will be most helpful Morphine sulfate 6 mg given hypodermically is also useful

Antibiotics Chloramphenicol terramycin aureomycin and streptomycin used in the dosage given in Chapter 1 are effective antibacterial agents in infections of the shigella organisms Since the infecting strain of the shigella sometimes develops resistance to the antibiotic being used and since there are variations in the susceptibility of individual strains to individual antibiotics it is advantageous to have these several antibiotics available Many more patients with bacillary dysentery, however, must be treated with different antibacterials different ones being used on patients with comparable degree of illness and infection with

faphthalidine None seems much if at all affected by penicillin Chloramphenicol terramycin and streptomycin are effective against some strains of salmonella For proper antibiotic therapy the infecting organism must be isolated and its susceptibility to the antibacterial agent determined The results of tests of susceptibility should be a guide in the selection of the antibacterial and should determine the dosage to be given as directed on page 24 If the infecting organism is found very slightly or not at all susceptible to these antibiotics as not infrequently happens then it seems useless to apply them in treatment These patients should be treated only by general measures as already described, with such local treatment as the nature of the infection indicates

Some value is claimed for a specific bacteriophage prepared from the infecting organism

Local treatment of purulent processes caused by members of the salmonella group should include drainage of pus instillation into the pus containing cavity of a solution of the antibiotic to which the organism is susceptible if it is found susceptible to any of them and possibly surgical excision Surgical treatment is obviously indicated for processes such as otitis media empyema pyelonephritis cholecystitis and appendicitis caused by salmonella organisms With salmonella meningitis if the infecting organism is susceptible to an antibiotic this should be given intrathecally in addition to its use intramuscularly or intravenously as described for other forms of meningitis (see p .4) provided a solution non irritating to the meninges is available Treatment of infection of the genito urinary tract with salmonella organisms is described under Pyelitis and Pyelonephritis

Carriers

There is no satisfactory treatment for salmonella carriers In general measures similar to those recommended for typhoid carriers are advisable In prophylaxis members of the salmonella group of bacteria may be added to other organisms commonly combined in typhoid paratyphoid vaccine and used as described in the section on Typhoid Fever the difficulty here is that the numerous salmonella organisms are far from immunologically identical

COLON BACILLUS INFECTIONS

Colon bacillus infections are clinically very like those of the salmonella group of organisms and treatment should be as described for the latter

5 SCOTT, R B BANKS I O and CRAWFORD R P Typhoid Fever in Children' *Arch Pediat*, 1950 LXVII, p 74
6 SMADEL J E BAILEY C A and LEWTHWAITE R Synthetic and Fermentation Type Chloramphenicol (Chloromycetin) in Typhoid Fever Prevention of Relapses by Adequate Treatment, *Ann Int Med*, 1950 XXXIII p 1
7 STRYKER H B Jr Failure of Chloramphenicol in a Chronic Typhoid Carrier *N E J Med*, 1950 CCXLII p 78
8 TYPHOID VACCINATION Queries and minor notes' *Jour Amer Med Assoc*, 1951 CXLVI p 1087
9 WOODWARD T E SMADEL J E and LEY H L Jr 'Chloramphenicol and Other Antibiotics in Treatment of Typhoid Fever and Typhoid Carriers *J Clin Invest*, 1950, XXIX, p 87

Salmonellosis

1 ROSS S BURKE F G RICE E C WASHINGTON J A, and STEVENS S Chloromycetin in the Treatment of Salmonella Enteritis, *N E J Med* 1950, CCXLII, p 173

Bacillary Dysentery

1 SCOTT L G Bacillary Dysentery and Gastro enteritis, *Delaware State Med J*, 1950 XXII, p 9
2 WIRTS C W Jr Acute Enteric Infections *Med Clin No Amer*, 1950 Nov p 1667

the same strain of organisms before it can be stated which antibacterial should be chosen to initiate treatment Sulfadiazine has the advantage of being much cheaper than any of the antibiotics and this should be taken into account by the physician Chloramphenicol seems more quickly effective than the other antibiotics but this statement admittedly is based on the comparative use of antibiotics on only a relatively small number of patients

Sulfonamide therapy is effective and considerably shortens the course of the disease The sulfonamides of choice are sulfadiazine and sulfa suxidine Sulfadiazine is to be given by mouth in an initial dose of 0 05 to 0 1 gm per kilogram of body weight followed by the same amount divided and given at 4 hour intervals over a period of 4 hours The higher dosage should be used in the more serious cases For adults the usual systemic doses of 0 to 4 0 gm followed by 1 0 gm every 6 hours until cure results and stool cultures are negative is satisfactory Sulfa suxidine may be given in an initial dose of 0 25 gm per kilogram of body weight followed by 0 25 gm per kilogram of body weight daily The total daily dose should be divided into 6 parts and given at 4 hour intervals For adults a satisfactory regimen consists of 5 to 7 gm followed by 3 gm every 4 to 6 hours Sulfonamide therapy must be continued until 3 stool cultures are negative Usually this therapy is required for 5 to 7 days Of the other sulfonamides mentioned sulfadiazine is preferable Sulfadimentine (Elkosin) shows promise and may prove more safe than sulfadiazine because of its lower incidence of renal complications It is given in a dose of 0 5 to 0 1 gm per kilogram of body weight

BIBLIOGRAPHY

Typhoid Fever

1 BRIGGS J N Relapse in Typhoid Fever after Treatment with Chloramphenicol *Lancet* 1950 1 p 115

2 CLAISSE M and CROSNIER J Perforation in the Course of Typhoid Fever Treated with Chloromycetin Healing by Only Medical Treatment *Presse Med* 1950 LVIII p 99

3 EL RAMLI A H Chloramphenicol in Typhoid Fever *Lancet* 1950 1 p 618

4 KNIGHT V RUIZ SANCHEZ F RUIZ SANCHEZ A SHULTZ S and McDERMOTT W Antimicrobial Therapy in Typhoid *Arch Int Med* 1950 LXXXV p 44

If aureomycin or terramycin is not effective, a combination of them with sulfadiazine or with streptomycin or dihydrostreptomycin should be given Dosage of sulfadiazine should be 1 0 gm every 4 hours after an initial dose of 4 0 gm together with alkalinization of the urine by giving sodium bicarbonate Dosage of streptomycin or dihydro streptomycin should be 2 0 gm daily divided into 2 intramuscular doses i e a dose every 12 hours day and night Because of possible toxic symptoms from this large dosage of streptomycin, it should usually not be continued for more than 4 to 7 days If toxic symptoms appear and are severe streptomycin should be stopped

Some still give Foshay s serum 20 cc intravenously or intramuscularly daily for 5 to 6 days after testing for skin sensitivity to this serum When it is used serum sickness often follows Its use is not advised

Chronic Brucellosis

For treating chronic cases a variety of therapeutic measures have been advised hyperthermia, transfusions of whole blood using if possible blood from an immunized donor transfusions foreign proteins, vaccine, antisera and brucellin aureomycin, chloramphenicol, terramycin, a combination of sulfadiazine and streptomycin Aureomycin should be tried first then terramycin if these are not successful sulfadiazine and streptomycin in combination should be given The dosage for these should be as stated under Acute Brucellosis In all cases prolonged bed rest and high caloric diet are important

Brucellin, a mixture of nucleoproteins derived from brucella organ isms in an alkaline solution has had wide application in the treatment of chronic cases with the claim of excellent results when the patients have high agglutinin titer and opsono cytophagic index It is a method of desensitization and unfortunately severe local and systemic reactions even with very small doses are frequent in many too severe to allow for continued use of brucellin Brucellin is given intracutaneously com mencing with a dose of 0 1 cc and increasing in increments of 0 1 to 0 2 cc at 5- to 7 day intervals until a dose of 1 0 cc is reached Brucellin may be tried if the antibiotics already described prove non curative

Some claim better results from bacterial vaccine than from brucellin particularly oxidized brucella vaccine preceded by sensitivity tests with very dilute material 1 120 000 This vaccine should be extremely dilute for the initial intracutaneous dose and should be continued by small

CHAPTER VIII

OTHER BACTERIAL DISEASES

Brucellosis

For discussion of treatment cases are divided into two groups acute and chronic each will be discussed separately

Acute Brucellosis

General measures as described in Chapter I should be applied Bed rest a nourishing diet and adequate fluid intake are indicated When *there is* arthralgia as *often* happens salicylates *as described for* Rheumatic Fever should be given When these patients sweat a great deal excess fluid intake is necessary to prevent dehydration judge the amount *needed by urine output which should be 1500 cc daily or more* Penicillin is not effective and so its use is not indicated Aureomycin streptomycin and terramycin are effective and should be tried

Aureomycin by mouth is advised for patients in the acute stage of brucellosis The recommended dose is 0.1 to 0.[illegible] gm divided and given every 6 hours After 1 or 2 days on this dosage the total daily amount is changed to 60 mg per kilogram of body weight divided into 4 doses From 8 to 12 hours after the first dose of aureomycin has been given an abrupt rise of temperature with a fall in blood pressure and tachycardia may occur apparently without any serious results and it is because *of these facts that the lower initial dose is advised Except for this* phenomenon aureomycin by mouth in this stated dosage seems to be non toxic Terramycin may be used instead of aureomycin in similar *dosage As for which one of these antibiotics will prove more* effective more frequently we must await reports of more cases

more units should be given On the basis of severity the following dosage of diphtheria antitoxin has been advised, intramuscularly for mild cases, 1,000 to 5,000 units for moderate cases 10,000 to 30 000 units for severe cases 50 000 to 100,000 units intravenously somewhat smaller doses are advised, as 5 000 to 15,000 units for moderate cases, 15,000 to 30 000 units for severe and 60 000 to 100 000 or more units for malignant cases For all severely ill patients intravenous antitoxin is preferable

It is very important to test the patient for horse serum sensitivity before giving any antitoxin this is done by injecting intradermally 0 2 cc of horse serum diluted 1 10 with normal salt solution, or 0 cc of antitoxin solution diluted 1 100 with normal salt solution If a reaction occurs desensitization of the patient with small intramuscular doses (0 1 to 0 2 cc) of antitoxin repeated at 15 to 20 minute intervals, is necessary before giving the therapeutic dose of antitoxin Goat-serum antitoxin can be used in place of horse serum antitoxin for patients sensitive to horse serum

Whenever a dose of diphtheria antitoxin is given it must be assumed that an anaphylactic reaction possibly a severe one may occur abruptly, and the physician must have at hand ready for immediate use, the preparations likely to control it At the first indication of a reaction 0 3 to 0 5 cc of a 1 1000 epinephrine (Adrenalin) hydrochloride should be given subcutaneously and repeated in 15 minutes if the reaction has not abated At the same time tripelennamine (Pyribenzamine) hydrochloride 50 to 100 mg should be given orally and the dose repeated at 15-minute intervals until a total dose of 150 to 200 mg has been given In addition the physician should be ready to give artificial respiration or better than this oxygen inhalation if severe respiratory difficulty develops as part of the anaphylactic reaction

It is customary now to give all severely ill patients and particularly those with the malignant form of diphtheria *diphtheria gravis*, penicillin in addition to diphtheria antitoxin as just described since penicillin has an antibiotic effect on both the diphtheria bacillus and on any complicating streptococci Penicillin dissolved in normal salt solution should be given intramuscularly or intravenously with an initial dose of 80,000 to 100,000 units followed at 3 hour intervals by half these amounts, continued until definite improvement is in evidence Some prefer to use penicillin in aqueous suspension intramuscularly in a daily dose of 300,000 to 600 000 units especially in less severely sick patients in addition to antitoxin dosage as already described Penicillin should always be used with diphtheria antitoxin not alone

increments in dosage given at 3 day intervals If reaction occurs dosage should be stopped and then recommenced using still smaller amounts

Still another approach to the treatment of this chronic disease has met with some success On the basis that transfused blood provided an immune mechanism builder, and that small doses of a sulfonamide appear to be just as effective as larger doses and less toxic the following program as advised by Huddleson may be tried The patient is placed at bed rest and begun on 0.5 gm of sulfadiazine every 4 hours around the clock On the first day of treatment he is also given 500 cc of compatible whole blood The dosage of sulfadiazine is continued at 0 25 gm every 4 hours for 7 days then reduced to 0 5 gm twice a day for additional weeks Such a course of treatment has been found to produce rather uniformly good results in over three fourths of a small series of cases that has been followed for nearly two years

One great deterrent to satisfactory results in this disease lies in the uncertainty of diagnosis except for patients with positive blood cultures In all probability many cases treated for brucellosis do not actually have the disease and so it is not surprising that the therapeutic results are not satisfactory

Prophylaxis consists of exercising care in the handling of animal products such as meat and avoiding the use of unpasteurized milk Infected animals should be diligently sought out and removed from the herds in a campaign similar to the anti tuberculosis program Vaccination of calves with the *Brucella abortus* strain 19 prepared as an attenuated viable culture apparently is of value in preventing development of cases in herds

Diphtheria

The most essential elements in satisfactory treatment of diphtheria are (1) early diagnosis by means of throat and nose cultures and (2) prompt dosage with an adequate amount of diphtheria antitoxin sometimes with the addition of penicillin It is best to give an initial large dose of *diphtheria antitoxin* intramuscularly for the average case intravenously for the severe case if improvement is not very striking at the end of 24 hours the antitoxin dose should be repeated The following doses of antitoxin are recommended for children up to 2 years 2 000 to 10 000 units from to 12 years 10 000 to 20 000 units over 12 years 20 000 to 50 000 units in malignant cases *(diphtheria gravis)* 100,000 or

Diet should be that already described for infectious diseases with fluid as needed to prevent dehydration, feeding by the nurse is essential if the patient has any difficulty in taking food, or if complete flat in bed rest is being enforced

If *pharyngeal paralysis* develops as a complication, probably only liquid food can be taken those patients should have the foot of the bed elevated 18 to 24 inches and the patient should be turned frequently from one side to the other to allow saliva and mucus to run freely from the mouth instead of going down the trachea If this happens, prompt resort to the suction apparatus to aspirate material from the larynx and trachea is essential If respiratory paralysis develops a *respirator* and the use of *oxygen* become necessary to prevent asphyxia

All diphtheria patients need frequent mouth cleansing and irrigation with a warm weakly alkaline solution or physiological salt solution to which penicillin may be added An ice bag on the neck is comforting to some patients, others prefer a warm application Acetylsalicylic acid, codeine phosphate or methadone should be used when pain from the throat or from headache is severe

In *cutaneous diphtheria* combining penicillin and diphtheria antitoxin has proved to be quite effective Of various methods of treatment, intramuscular diphtheria antitoxin in doses of 20 000 to 50,000 units and continuous wet packs of penicillin to the skin lesions 500 to 1000 units per cc have given excellent results Penicillin has an action against the diphtheria bacillus locally and is likewise most effective against the secondary infection usually present Unfortunately, topically applied penicillin may cause a sensitivity reaction so care must be taken in such applications Bacitracin may be substituted for the penicillin, it has a low index of topical sensitivity A solution containing 500 units per cc should be used Bacitracin ointment containing 500 units per gram, may also be used

Patients who have had diphtheria are to be *kept in isolation* until they have had not less than 2 throat cultures negative for diphtheria bacilli Normally the first release culture should not be taken until at least one week after the onset of the disease If the second culture is positive, a period of 5 days should elapse before taking another culture In the majority of cases organisms disappear from the nose about a week after the membrane disappears Children should not return to school until at least 3 weeks have elapsed since the onset of the illness and until throat cultures are negative The same applies for cultures from cutaneous lesions If cultures remain positive, the isolated organisms must

Every physician who undertakes to treat diphtheria should be able to perform *intubation* on his patient and have ready for immediate use the needed intubation instruments in case laryngeal obstruction develops or failing that have quickly available a consultant who can carry out intubation If the obstruction is lower down in the trachea *tracheotomy* should be available quickly if the need arises, usually tracheotomy requires a surgical consultant

In addition to diphtheria antitoxin and penicillin as just described the *general measures* appropriate to all infectious diseases as described in Chapter 1 should be applied with emphasis on isolation and especial attention given to avoiding contact with the patient s face particularly when the patient coughs Everything coming in contact with the patient must be sterilized or destroyed Nurses and other attendants should wear face masks cover their hair and use a sterilized overgarment

Nurses and others in contact with the patient should have a Schick test to ascertain their susceptibility to infection This is done by injecting intracutaneously into the inner aspect of the forearm 1/50 of a M L D *of diphtheria toxin diluted to 0 1 cc with physiological salt solution* A positive reaction is indicated by a reddish brown raised indurated area with occasional vesicle formation which appears within 24 hours and remains 5 to 7 days before beginning to fade A scaling brownish wrinkled area may remain for 5 to 6 weeks Pseudo reactions usually disappear by the fifth day A control test may be performed on the other arm by injecting the same dose of a previously heated toxin at the time and in the same manner as the active toxin Pseudo reactions can then be determined promptly

Non immune contacts as shown by the Schick test should be observed closely and if early signs of the disease appear suitable amounts of antitoxin should be given and measures instituted to treat the diphtheria infection

When non immune contacts cannot be observed closely and given early treatment passive immunization is advisable Usually 1000 to 000 units of antitoxin is sufficient and will give protection for approximately 3 weeks Active immunization should then be carried out Penicillin 300 000 to 600 000 units by mouth given before meals or procaine penicillin in aqueous suspension 300 000 units given intramuscularly each day is also protective and should be taken by the non immune

Bed rest is very important and should be complete with the patient flat in bed and allowed the least possible amount of physical activity if he is severely ill and/or if there are any signs of cardiac involvement

until local lesions heal Fever usually disappears by the third day of treatment Acutely ill patients and those who are not able to take aureomycin by mouth should be given streptomycin Streptomycin, although somewhat more toxic, will give good results in a daily dose of 3 0 gm It is administered intramuscularly in divided doses of 0 5 gm every 4 hours around the clock for 7 days — in resistant cases for 10 days

Under antibiotic treatment the bubo of tularemia may respond slowly or even break down and slough Incision is not advised and antibiotic therapy should be continued If secondary infection develops, local bacitracin solution is recommended, 500 units to the cc, and this should be applied also to any ocular lesions that may be present

If nausea or vomiting is caused by either of the antibiotics, the administration of 0 3 gm of sodium bicarbonate at the time of each dose may be tried If symptoms persist dimenhydrinate (Dramamine) in an oral dose of 50 mg should be given and, if nausea continues, repeated 1 hour after the first dose

During the acute febrile stage bed rest an adequate and nourishing diet, free fluid intake, and acetylsalicylic acid are indicated

The prognosis with antibiotic treatment is excellent, although occasionally convalescence may be prolonged

Prevention of tularemia is most important and is simply a matter of taking strict precautions Anyone skinning rabbits, chiefly of the wild variety should wear rubber gloves during the procedure, and all rabbit meat should be cooked thoroughly before being eaten Laboratory workers handling the organisms are liable to contract the disease and should wear face masks for protection

Asiatic Cholera

As Asiatic cholera usually occurs in epidemic form with many patients acutely and seriously ill proper treatment of individual cases is difficult to carry out Many omissions and compromises from what can be called the ideal treatment are usually inevitable Methods to protect those not already infected should be stressed above all else

Treatment The most important parts of treatment are absolute bed rest and the prevention of dehydration In Asiatic cholera vomiting and diarrhea cause an enormous loss of fluid and salt from the body, which should be replaced promptly to prevent the marked dehydration and loss of fixed base the cause of death in so many of the patients As

be tested for virulence if it is found avirulent isolation may be ended Usually penicillin treatment shortens the period during which organisms are found If they persist after the acute phase penicillin by mouth 300 000 to 600 000 units daily divided into 3 doses and given before meals or procaine penicillin intramuscularly 300 000 units daily, hastens the disappearance of the organisms

In *prophylaxis* all who have had a positive Schick test should be immunized with alum precipitated toxoid receiving subcutaneously 0 5 1 0 and 1 0 cc at intervals of 1 to 2 months and another 1 0 cc a year later Increasingly all children irrespective of a positive Schick test are being immunized with alum precipitated toxoid Adult patients should be tested first by an intradermal injection of 0 1 cc of the toxoid (*Maloney reaction*) if there is a marked reaction smaller doses of the toxoid should be used in immunizing

Carriers Many diphtheria patients harbor diphtheria bacilli in throat and nose for 2 or 3 weeks after they are well of the disease, some for longer periods and some continuously These constitute carriers of which the chronic carriers are particularly important as spreaders of the disease Treatment of carriers to clear their upper respiratory tracts of virulent diphtheria bacilli has been unsatisfactory in the past Antiseptic solutions applied locally are not satisfactorily effective In some but not in all chronic carriers tonsillectomy and adenoidectomy have been effective The use of penicillin along with diphtheria antitoxin in treating acute diphtheria seems to shorten the period of persistence of diphtheria bacilli in the throat and nose and to reduce the number of carriers If virulent organisms persist penicillin 300 000 to 600 000 units by mouth divided and given before meals or penicillin procaine in aqueous suspension 300 000 units intramuscularly daily should be given for 10 days to 2 weeks If this fails aureomycin chloramphenicol terramycin or streptomycin should be given a trial

TULAREMIA

At present aureomycin chloramphenicol and streptomycin are effective antibiotics for the treatment of tularemia Aureomycin 25 to 50 mg per kilogram of body weight divided and given in 4 daily doses or 0 5 to 1 0 gm by mouth every 6 hours the larger dose for the more acutely ill patients gives excellent results This dosage should be continued for at least 5 days after the temperature has reached normal or

should be accompanied by frequent observations of the urine to detect red cells and/or the development of anuria Keeping the urine alkaline with additional sodium bicarbonate may help prevent these occurrences If these changes do result from the sulfonamide, it should be stopped at once Sulfisoxazol (Gantrisin) or sulfadimetine (Elkosin), which cause less renal toxicity than sulfadiazine should be tried in the same dosage as recommended for sulfadiazine Until these several antibacterial drugs have had extensive application it is impossible to say which of them will be most effective

Azotemia may develop in patients with Asiatic cholera, either with or without sulfonamide therapy Repeated determinations of blood urea or non protein nitrogen will show considerable increase if azotemia is developing Then efforts should be made to increase urine output and any sulfonamide should be stopped

No drug treatment beyond what has been indicated is needed Digitalis or so called cardiac stimulants should not be used, even if there is circulatory collapse they seem to do no good and may do harm

Diet should include as much fluid as possible — plenty of fruit juices in addition to eggs and milk and any other food in liquid form Supplementary vitamins of the B complex and vitamin C should be given As a rule, very little food will be taken until convalescence begins except by those only mildly sick with the disease because of the nausea and vomiting that afflict the sicker patient As severe illness usually results in death after not more than 5 days, diet beyond fluids is no serious problem

Complications are infrequent and require only treatment appropriate for the etiology Thrombosis of leg veins must be watched for, and if it occurs treatment by vein ligation is indicated to prevent pulmonary embolism

Convalescence is usually rapid Gradual return to a normal diet is indicated Patients should be kept under observation until stool cultures no longer show cholera vibrios

Prophylaxis Those in contact with the patient should be protected by vaccination and should wear gowns and head coverings that can be sterilized after use Face masks are desirable as a means to keep fingers from contact with the mouth Hands should be washed thoroughly and soaked in an antiseptic solution 1 1000 tincture of benzalkonium (Zephiran) chloride or 1 10 000 bichloride of mercury, after each period of contact with the patient All excreta of the patient and things contaminated by excreta should be sterilized by boiling, burning,

nausea and vomiting greatly restrict fluid intake by mouth except in mild cases the physician should immediately resort to giving fluid intravenously Fluids warmed to body temperature should be given slowly and continuously or repeatedly in large amounts the total amount to be judged by the specific gravity of the blood Blood specific gravity should be tested often by the copper sulfate droplet technique and should be kept at or near to 1 058 This may require as much as 10 000 cc of fluid in 24 hours

Normal saline solution or a hypertonic solution containing 13 75 gm sodium chlordie and 0 5 gm calcium chloride per liter should be given not blood Since acidosis is usual in these patients sodium bicarbonate is also needed with the first 1000 cc of normal saline solution it is advisable to give 300 cc of a per cent solution of sodium bicarbonate and this should be repeated several times a day The presence of acidosis in Asiatic cholera is not usually indicated by ketone bodies in the urine as it is in the acidosis of diabetes mellitus but must be detected by determinations of blood or carbon dioxide combining power if such testing is available If acidosis does develop as shown by these tests more sodium bicarbonate solution should be given or in its place one sixth molar solution of sodium r lactate can be used

To the normal saline solution should be added glucose to make a 5 per cent solution but not more than 400 gm of glucose should be given each 24 hours Also thiamin chloride should be added to the glucose-normal saline solution, 1 mg for every 25 gm of glucose

Severe vomiting may be ameliorated by the oral administration of a dilute solution of cocaine containing 8 0 mg of cocaine hydrochloride Pain from muscle cramps may be treated with quinine hydrochloride 0 6 gm given intravenously dissolved in 300 to 400 cc of saline solution Meperidine hydrochloride 50 to 100 mg or methadone 5 to 10 mg given intramuscularly will also be effective

Next in importance to preventing dehydration should be the elimination of the cholera vibrios Penicillin is ineffective Aureomycin chloramphenicol terramycin and streptomycin are effective At the present time chloramphenicol is apparently giving the best results It should be given in a dose of 60 to 75 mg per kilogram of body weight as an initial dose followed by 60 mg per kilogram daily divided and given in 4 doses at 6 hour intervals Sulfadiazine has given good results and may be given if the antibiotics do not give immediate benefit The initial dose of sulfadiazine should be 3 or 4 gm Since these patients have a small output of concentrated urine dosage particularly with sulfadiazine,

100 cc is of value and should be given in conjunction with the strepto mycin or given alone if for any reason the streptomycin cannot be given If the patient is not responsive, aureomycin, chloramphenicol or terramycin should be substituted for streptomycin Penicillin is usually ineffective

Local buboes are to be treated with hot applications, and when fluctuation appears they should be incised and drained Meperidine (Demerol) hydrochloride 50 to 100 mg methadone, 5 to 10 mg, or morphine sulfate, 8 to 15 mg, may be given subcutaneously at 3 hour intervals for severe pain

Prophylaxis Vaccination with a vaccine prepared from the killed *P pestis* organism 0 5 cc subcutaneously, followed by 1 0 cc in a week to 10 days and later a supplementary dose of 1 0 cc at the end of 6 months or at a time of a suspected exposure gives definite protection This vaccine should be given to all who are likely to be exposed Elimination of rodents from human habitations and destruction of fleas and lice by dusting and spraying contaminated areas with chlorophenothane [DDT] are essentials in the prevention of this disease At the first suspicion of plague the public-health authorities should be informed, bacterial studies made and a definite diagnosis established Isolation must be rigidly enforced and therapy started promptly Known contacts should be given 2 to 3 gm of sulfadiazine sulfadimetine (Elkosin), sulfisoxazol (Gantrisin) or sulfamerazine daily for 5 days

Friedlanders Bacillus (Klebsiella) Infections

Infection with this organism may be of many different varieties with differences in response to treatment Entry into the body may be through the nose and throat genito urinary tract, intestines or middle ear Thus the Friedlander s bacillus *(Klebsiella pneumoniae)* can cause an infection in the lungs peritoneum, and other serous cavities the meninges liver, or kidneys from any of these may develop widespread infection with septicemia and endocarditis Differences in response to treatment are best exemplified perhaps in the lungs where an acute pneumonia may be overcome readily while a chronic infection may lead to abscess and fibrosis with resistance to therapy

Friedlander s bacillus is a pus former in many patients, and hence any accumulation of pus should be drained surgically if accessible Moreover

or with chemicals as described under Typhoid Fever Patient s clothing bedding, and eating utensils and gowns and head coverings of attendants should be sterilized after use by boiling or in a steam sterilizer

In case of epidemic the population should be protected with a vaccine containing 8000 million killed cholera vibrios per cc the dosage of this should be 0 5 cc subcutaneously, followed by a second dose of 1 cc in 7 to 10 days If possibility of exposure continues revaccination with 1 cc should be repeated every 4 to 6 months Water should be boiled before drinking and no uncooked fruit or vegetables should be eaten during the presence of cholera in the community The water supply if possible should be heavily chlorinated unfortunately this is not entirely satisfactory in eliminating cholera vibrios and should not replace boiling the drinking water

Carriers should be sought out by bacteriological examinations of stools for cholera vibrios and the carriers should be isolated while undergoing protective vaccination It seems wise to give them an antibacterial as described in the preceding section on treatment Supervision should be continued until carriers have stools free of vibrios Food handlers should be thoroughly and repeatedly studied bacteriologically to detect carriers and every effort made to detect as early as possible any evidence of cholera disease in them

Plague

Pasteurella pestis infections are so severe and run such a rapid course that therapy must be instituted early and pursued with vigor to obtain optimal results The high mortality rate especially in the pneumonic type makes it imperative that the disease be prevented whenever possible

Treatment Bed rest and supportive measures in the form of hydrotherapy for high fever intravenous fluids for dehydration 5 to 10 per cent glucose solution intravenously and plague immune serum 100 to 00 cc should be given immediately

Streptomycin or dihydrostreptomycin has proved highly effective against *P pestis* infections and should be given promptly Intravenous administration of a dose of 1 to 2 gm every 24 hours dissolved in 2000 to 4000 cc of normal saline solution is recommended as the initial dose to be followed by 4 gm divided into 6 or 8 intramuscular doses every 24 hours until the temperature has been normal for 3 days Sulfadiazine in sufficient dosage to maintain a blood level of from 12 to 15 mg per

100 cc is of value and should be given in conjunction with the streptomycin or given alone if for any reason the streptomycin cannot be given If the patient is not responsive aureomycin, chloramphenicol, or terramycin should be substituted for streptomycin Penicillin is usually ineffective

Local buboes are to be treated with hot applications and when fluctuation appears they should be incised and drained Meperidine (Demerol) hydrochloride, 50 to 100 mg methadone, 5 to 10 mg, or morphine sulfate 8 to 15 mg may be given subcutaneously at 3 hour intervals for severe pain

Prophylaxis Vaccination with a vaccine prepared from the killed *P pestis* organism 0 5 cc subcutaneously followed by 1 0 cc in a week to 10 days and later a supplementary dose of 1 0 cc at the end of 6 months or at a time of a suspected exposure, gives definite protection This vaccine should be given to all who are likely to be exposed Elimination of rodents from human habitations and destruction of fleas and lice by dusting and spraying contaminated areas with chlorophenothane [DDT] are essentials in the prevention of this disease At the first suspicion of plague the public health authorities should be informed bacterial studies made and a definite diagnosis established Isolation must be rigidly enforced and therapy started promptly Known contacts should be given 2 to 3 gm of sulfadiazine, sulfadimetine (Elkosin) sulfisoxazol (Gantrisin) or sulfamerazine daily for 5 days

FRIEDLANDERS BACILLUS (KLEBSIELLA) INFECTIONS

Infection with this organism may be of many different varieties with differences in response to treatment Entry into the body may be through the nose and throat genito urinary tract intestines or middle ear Thus the Friedlander s bacillus *(Klebsiella pneumoniae)* can cause an infection in the lungs peritoneum and other serous cavities the meninges liver, or kidneys from any of these may develop widespread infection with septicemia and endocarditis Differences in response to treatment are best exemplified perhaps in the lungs where an acute pneumonia may be overcome readily while a chronic infection may lead to abscess and fibrosis with resistance to therapy

Friedlander s bacillus is a pus-former in many patients and hence any accumulation of pus should be drained surgically if accessible Moreover

if the urinary or biliary tract is obstructed the obstruction should be removed if best results are to be obtained from treatment

Aureomycin streptomycin and terramycin are the drugs of choice of Friedlander's bacillus infections although the results are not always uniformly satisfactory Aureomycin or terramycin is preferable to streptomycin and the initial dose should be large A daily dose of 4.0 gm divided into 8 equal doses may be given 1.0 gm every 4 hours may even be desirable Streptomycin should be given by intramuscular injection in a dose of 2.0 to 4.0 gm daily Cavities infected with this bacillus should be irrigated with antibiotic solution

The sulfonamide sulfadiazine has been found to be effective in Friedlander's bacillus infections Because of the potential severity of these infections when sulfadiazine is used treatment should begin with 6 gm of the sodium salt given intravenously as a 5 per cent solution and this dose should be repeated in 12 hours to maintain a high blood level of the drug When the infection is under control oral medication may be begun 1.5 to 2.0 gm of sulfadiazine being given every 4 to 6 hours

Sulfadimetine (Elkosin) and sulfisoxazol (Gantrisin) are also effective and show less tendency to cause renal irritation An initial dose of 4 to 6 gm followed by 1 to 2 gm every 4 hours is recommended For children a daily dose of 0.1 gm per kilogram of body weight is advised

To obtain the best results in severe and fulminating infections antibacterials should be combined using the full dosage of each drug Penicillin has not been effective in treating Friedlander's bacillus infections

Of the several serological types of Friedlander's bacillus a specific antiserum has been developed for type A the results of which when used alone in treatment have been largely disappointing It may be combined effectively with chemotherapy however as already described, particularly in more severely ill patients

Tetanus

The patient with symptoms of tetanus must be considered an emergency case and every effort should be made to prevent and give relief from the spasm and pain until tetanus toxin is neutralized and infection with *Clostridium tetani* is eliminated He should be on complete bed rest in a darkened quiet room well protected from annoying external stimuli

Adequate nutrition and fluid balance must be maintained If laryngeal spasm is present and not relieved by antispasmodic therapy the patient

should be fed by stomach tube or be given adequate fluid and nutrition parenterally Blood transfusions or plasma may be needed Severe laryngeal spasm causing suffocation requires tracheotomy

Immediately after the diagnosis of tetanus has been made the patient should be tested for serum sensitivity and if not sensitive a dose of 50 000 to 60,000 units of tetanus antitoxin intravenously and 20,000 to 40 000 units intrathecally should be given Injections should be slow and a syringe containing 1 0 cc of 1 1000 epinephrine (Adrenalin) hydro chloride should be ready for emergency use Patients showing sensitivity should be desensitized as described under Diphtheria The large initial intravenous injection should be followed by daily intravenous injections of 5000 units of tetanus antitoxin in order to neutralize any additional toxin that may be formed in the wound Intrathecal injections of 15,000 units should be repeated daily for the first few days and then reduced to injections every other day

The wound site and adjacent soft tissue should be infiltrated promptly with 10 000 units of tetanus antitoxin After 1 hour the wound should be excised widely and careful debridement carried out The wound should be irrigated with a zinc peroxide suspension of proper consistency to penetrate all parts and then compresses soaked with zinc peroxide applied The compresses should be renewed every 12 hours Penicillin, 50 000 units intramuscularly every 3 hours should be started immediately and continued until the patient is symptom free If the wound is infected with an organism sensitive to an antibiotic other than penicillin that antibiotic in proper dosage should be given as well

Sedation is most helpful and should be continued as long as symptoms indicate need for it It should not be so vigorous that it depresses res piration and blood pressure or abolishes the cough reflex Chloral hydrate 2 to 3 gm or paraldehyde 10 to 40 cc well diluted with water or fruit juice and given by mouth is excellent These drugs may also be given by rectum in the same dose well diluted with water or olive oil Some patients respond better to the barbiturates and in these patients sodium pentobarbital 0 2 to 0 3 gm or sodium phenobarbital 0 2 to 0 3 gm , given as a 5 per cent solution and repeated at 3 or 4 hour intervals is recommended Basal anesthesia with tribromethanol (Avertin with Amylene Hydrate) 30 to 60 mg per kilogram of body weight 1 or 2 times a day, is most helpful and gives effective sedation for 2 to 4 hours

Spasm and muscular rigidity may be ameliorated greatly by the use of d tubocurarine chloride magnesium sulfate or mephenesin (Tolserol) The most effective of these agents and also the most toxic is d tubocura

rine chloride Administration should be done by an individual familiar with its use Patients vary considerably in their reaction to this drug consequently the initial dose should be smaller than subsequent doses For prompt action the aqueous solution containing 3 0 mg d tubocurarine chloride equivalent to 0 units per cc should be given intravenously For patients having convulsions or severe spasms a dose of ½ units per pound of body weight is recommended The initial dose should be 20 units less than the calculated dose The patient under ether or avertin anesthesia or heavy sedation should be given a dose of 0 units initially and thus increased as patient s response indicates Injection should require 1 to 1½ minutes, and the patient should be observed carefully for evidence of toxicity especially respiratory failure Neostigmine (Prostigmine) methyl sulfate 1 000 solution should be available for immediate use and if evidence of mild respiratory embarrassment appears 1 cc should be given intravenously Atropine sulfate 0 6 mg should be given if undesirable reactions to neostigmine appear such as excessive bronchial secretion intestinal cramps and diarrhea Should respiratory failure occur the respiratory passages should be cleared and artificial respiration and oxygen given If the initial smaller dose is tolerated well the calculated dose may be given in subsequent injections The effect of the drug lasts for 0 to 60 minutes and when indicated should be repeated

Intramuscular administration is effective for the patient not requiring immediate curarization A dose of ½ to ¾ unit per pound of body weight is satisfactory This dose may be repeated 3 or 4 times a day when indicated

For long continued uniform action in these patients d tubocurarine *chloride suspended in peanut oil and wax containing 27 mg equivalent* to 180 units per cc is excellent This preparation is given in an initial dose of 108 units in the gluteal muscles Relaxation should be apparent within 1 to 3 hours and be maintained for 18 to 4 hours Subsequent injections as indicated by the clinical response of the patient can be increased by 36 units to a daily injection of 360 units

Magnesium sulfate affords considerable relaxation and is not as toxic as d tubocurarine chloride It should be given intramuscularly as a 5 per cent solution in a dose of 1 to 2 cc for each 0 pounds of body weight 4 times in 4 hours Should respiratory depression or other toxic symptoms develop they can be relieved promptly by injecting intravenously 10 to 0 cc of a 5 per cent solution of calcium chloride in

physiological saline Injections of magnesium sulfate should be continued until symptoms disappear

Patients exhibiting mild to moderate degrees of spasm and pain receive effective relief from mephenesin (Tolserol) in a dose of 1 to 3 gm orally 3 to 6 times a day In the more serious cases with moderate to severe spasm, the drug may be given intravenously or intramuscularly in a dose of 1 0 gm dissolved in 20 cc of physiological saline and repeated at 6 to 12 hour intervals as indicated by the patient's symptoms Intravenous injection should be slow and the patient must be observed carefully Satisfactory therapeutic levels may produce nystagmus, blurring of vision, and dryness of the mouth Occasionally hemoglobinuria follows intravenous medication Better results are obtained with mephenesin if it is combined with phenobarbital sedation in a dose of 0 2 to 0 3 gm 1 to 3 times a day

Prevention The best treatment of tetanus is its prevention Individuals likely to have wounds contaminated by soil, such as farmers, mechanics soldiers, and children and allergic individuals likely to be sensitive to horse serum or those known to be allergic to horse serum should be actively immunized against tetanus This is best done with refined alum precipitated toxoid, which gives less reaction than plain toxoid The best protection is afforded by 2 injections of 0 5 to 1 0 cc, depending on the instructions given on the vial s label, given subcutaneously at 4- to 6-week intervals A subsequent booster dose of 1 0 cc of the alum precipitated toxoid should be given subcutaneously at the end of 1 year The immunity produced lasts 2 or 3 years A booster dose should be given when a previously actively immunized individual receives a wound contaminated with soil Immunity should be maintained by supplemental injections of one immunizing dose after one year, and then at 5-year intervals

A patient receiving extensive abrasions deep cuts, macerated or puncture wounds contaminated with soil should be treated as having been exposed to tetanus The wound should be opened thoroughly, cleaned and all foreign matter and dead tissue removed It should then be irrigated thoroughly with zinc peroxide suspension of proper consistency to penetrate to all parts of the wound and packed with gauze saturated with the zinc peroxide The dressing should be renewed every 12 to 24 hours If infection appears in the wound the appropriate antibiotic as determined by organism sensitivity should be given Those previously actively immunized should be given a booster dose of alum precipitated toxoid Patients not previously actively immunized or

in whom the status of immunization is not known should be passively immunized by giving them subcutaneously 1500 to 2000 units of tetanus antitoxin after first checking for sensitivity to the serum This protection lasts for approximately 7 to 10 days The patient should then be actively immunized since sensitivity to the serum usually develops and makes subsequent passive immunization much more dangerous Patients exhibiting sensitivity to the serum should be desensitized as described under Diphtheria

Gas Bacillus Infection Bacterial Gas Gangrene

The group of gram positive bacilli the clostridia are prevalent in nature and in man cause local infection usually beginning in a local trauma with gas production in the tissues and/or septicemia sometimes with widespread gas production Both treatment and prevention will be discussed

Treatment For *local infections* treatment should consist of intra muscular or intravenous injections of polyvalent gas gangrene antitoxin and penicillin and wide open surgical drainage with extensive debride ment of injured tissues

The minimum therapeutic dose of trivalent gas gangrene antitoxin contains 10 000 units of *Clostridium perfringens (welchi)* and *Cl septicum* and 1500 units of *Cl oedematiens (novyi)* the dose of penta valent antitoxin contains in addition 3000 units of *Cl histolyticum* and 1500 units of *Cl bifermetans (sordelli)* either may be used intramus cularly or intravenously 1 or 2 doses every 1 hours with the usual precautions against anaphylactic reactions Injection of antitoxin into the local tissues is advised as is the application of bacitracin and pen- icillin locally Aureomycin chloramphenicol and terramycin may be used in full dosage, but they are inferior to penicillin Terramycin shows promise and in serious cases may be given intravenously in a dose of 0 25 to 0 5 gm every 12 hours as indicated Streptomycin is of no bene fit in these infections

Penicillin in aqueous solution should be given intramuscularly or intravenously every 3 hours in amounts totaling not less than 1 000 000 units each 24 hours Both antitoxin and penicillin should be continued until temperature is normal and signs of toxemia have disappeared In severe infections it is advisable to supplement antitoxin penicillin therapy with large doses of terramycin or sulfadiazine Aureomycin should be

given in full dosage if the infection is not responding to penicillin, sulfadiazine or terramycin

Local infections should be opened promptly by extensive incisions with widespread debridement of injured and involved tissues and local application of dressing soaked with normal saline solution containing 400 units of penicillin or 500 units of bacitracin or terramycin per cc

For the *septicemic form* antitoxin penicillin terramycin, and sulfadiazine as already described should be given in large doses, if there is in addition any local infection this should also be treated as already described

If anemia develops as often happens repeated *blood transfusions* are indicated

General measures as described for infectious diseases in the first section should be applied also

Prophylaxis Prompt surgical treatment with incision and drainage should be given local wounds with any probability of becoming infected with any of the group of clostridia, particularly if the wound was inflicted in or about barns through dirty clothing and where bits of soil may have been carried in Local applications of bacitracin ointment and intramuscular injections of 300 000 units of procaine penicillin daily for 3 or 4 days are advised for all such traumata Search for gram-positive bacteria should be made of any discharge from such wounds if found antitoxin and penicillin should be used at once as described in the section on Treatment Prophylactic use of gas gangrene toxoid, to be used as described under Tetanus is advised for those liable to traumata with a probability of infection with clostridia If the individual has had toxoid a booster dose should be given as soon as trauma as described in the first sentence of this section has occurred

ANTHRAX

Local anthrax, so called malignant pustule should be treated with a minimum of manipulation and complete rest the part should be immobilized and the patient kept in bed Incision excision and cauterization should not be done The local wound should be covered with a wet dressing of penicillin of the strength of 400 units per cc or bacitracin 500 units per cc Also the specific antianthrax serum and penicillin should be used as described for the various internal forms of anthrax and for septicemic anthrax Aureomycin chloramphenicol or terra

mycin in usual doses are also effective in cutaneous anthrax However, they are not as effective as penicillin and possibly sulfadiazine Sulfadiazine may be used in addition when the lesion is an active and severe one Pain may be controlled with salicylates codeine or methadone

For internal anthrax such as the gastro intestinal pulmonary and meningitic forms the specific antianthrax serum should be given with the needed precautions against possible anaphylactic reactions as described for the use of antitoxin in Chapter I the serum should be given intravenously slowly in doses of 300 cc repeated in 6 to 12 hours as indicated by its effects on symptoms

In addition penicillin should be given intravenously in large doses at 3 hour intervals to total not less than 1 000 000 units each 4 hours preferably much more since internal anthrax usually has a high mortality if not treated promptly and very thoroughly If there is meningeal involvement — anthrax meningitis — penicillin should also be given intrathecally following lumbar puncture and drainage of spinal fluid as described for meningococcic meningitis Sulfadiazine 4 gm initially followed by 1 0 gm every 4 hours is recommended in conjunction with penicillin in severe fulminating cases and especially for those exhibiting meningeal involvement

General measures for the treatment of infectious diseases should be used for all patients Destroy or thoroughly sterilize all dressings or anything possibly infected with anthrax bacilli remembering that the anthrax bacillus is a spore bearing organism and that its spores are very resistant Caps gowns and masks should be worn by those in contact with the pulmonary cases

Prophylaxis Since anthrax in man almost always results from handling hides horse hair or wool these should be sterilized as far as possible and those handling them should be protected by gloves and aprons and should work in rooms where proper ventilation will carry off dust Protective vaccination has been suggested but so far has not been developed or used enough to justify recommendation

GLANDERS

Early recognition isolation and prompt treatment are essential to proper therapy of glanders If the lesion is a local skin involvement the part should be immobilized water soluble sulfadiazine ointment should be applied and sulfadiazine should be given in full dosage for its systemic

effect Acute or chronic systemic glanders should receive full dosage of sulfadiazine Bed rest and supportive measures to control fever, pain, and dehydration are indicated in all cases Chemotherapy should be continued for a total of 3 weeks Penicillin is of limited value but should be given as supplementary therapy Streptomycin has proved to be effective against cultures of the organism and has given excellent clinical results in acute glanders

Melioidosis

This has been a highly fatal disease, clinically similar to glanders and tularemia Since fleas and rodents may transmit the *Pfeifferella Whitmori*, the patient should be isolated and these factors guarded against The chills high fever and multiple abscesses call for heroic measures in symptomatic care highly nutritious diet, and fluids to prevent dehydration Recently the causative organism has been found to be quite sensitive to sulfadiazine in vitro 5 gm of the sodium salt should be given intravenously, with subsequent intravenous doses at 12 hour intervals or 1 0 to 1 5 gm by mouth every 4 hours to maintain a blood level of drug of 15 mg per 100 cc Penicillin has been found to be ineffective in vitro and in vivo Streptomycin as in glanders, may prove effective, sulfadiazine failing, it should be tried

Haverhill Fever

Streptobacillus moniliformis infection is best treated by the prompt administration of 300 000 units of penicillin procaine fortified with 100 000 units of soluble penicillin every 12 hours for 1 week and streptomycin 2 gm daily given in divided doses at 6 hour intervals for 4 or 5 days The measures described in Chapter 1 should also be applied Mild cases frequently respond to penicillin or streptomycin used alone The sulfonamides are of very little value

Listerellosis

Therapy consists of the general measures described in Chapter I and the prompt administration of chloramphenicol or aureomycin in fairly large dosage Sulfadiazine is also helpful If there is a meningeal involve-

ment with increased spinal fluid pressure lumbar puncture with gradual withdrawal of fluid and release of pressure is indicated

BIBLIOGRAPHY

Brucellosis

1 DOWLING H Combination of Aureomycin and Streptomycin the Most Effective Method Available Today for Treatment of Brucellosis *Antibiotics and Chemotherapy* 1951 1 p
2 GRIGGS J F Chronic Brucellosis Follow Up Study of 133 Patients Treated with Oxidized Vaccine *Calif Med*, 1948 LXIX p 205
3 HARRIS H J Aureomycin and Chloramphenicol in Brucellosis *Jour Amer Med Assoc* 1950 CXLII p 161
4 HERRELL W E and BARBER T E New Methods for the Treatment of Brucellosis *Jour Amer Med Assoc* 1950 CXLIV p 519
5 SPINK W W Studies on Brucellosis in Minnesota *Minn Med* 1950 XXXIII p 333

Diphtheria

1 HEWITT L F Use of Antibiotics in Treatment of Experimental Diphtheria Infections *Brit J Exp Path* 1950 XXXI p 597
2 KARELITZ S and SPINELLI V A Penicillin Treatment of Diphtheria Carriers *J Pediat* 1949 III p 639

Tularemia

1 FOSHAY L Treatment of Tularemia (Especially Streptomycin) *Postgrad Med* 1948 IV p 315
2 HUNT J S Pleuropulmonary Tularemia 1 Cases Treated with Streptomycin *Ann Int Med* 1947 XXVI p 263
3 LONG P H CHANDLER C A BLISS E A BRYER M S and SCHOENBACH E B Use of Antibiotics *Jour Amer Med Assoc* 1949 CXLI p 315
4 MORGAN H J Pleuropulmonary Tularemia (Streptomycin Therapy) *Ann Int Med* 1947 XXVII p 519
5 PARKER R T LESTER L M BAUER R E HALL H E and WOODWARD T E Use of Chloramphenicol (Chloromycetin) in Experimental and Human Tularemia *Jour Amer Med Assoc*, 1950 CXLIII p 7

6 TAYLOR R R Report on Tularemia Its Diagnosis and Treatment *J Arkansas M Soc* 1950 XLVII, p 47
7 WOODWARD T E PARKER R T and HALL H E Therapeutic Results with Aureomycin and Chloramphenicol *Bull N Y Acad Med* 1950 XXVI p 66

Asiatic Cholera

1 COLLIER H O J HALL L I and WATERHOUSE P D 'Studies in Chemotherapy of Cholera Laboratory Evaluation of Remedies for Cholera *Ann Trop Med* 1949 XLIII, p 155
2 GAULD H L SCHLINGMAN A S JACKSON E B MANNING M C BATSON H C and CAMPBELL C C Chloramphenicol (Chloromycetin) in Experimental Cholera Infections *J Bact* 1949 LVII p 349

Plague

1 ESTRADE F First Cases of Cure of Primary Pneumonic Plague Obtained with Streptomycin *Presse Med*, 1951 LIX p 328
2 GHOSH P K Outbreak of Plague in Epidemic Form Treated with Streptomycin and Sulfadiazine *Indian Med Gaz*, 1950, LXXXV p 441
3 LINK V B Plague *Jour Amer Med Assoc* 1950 CXLIV, p 375

Friedlander s Bacillus Infections

1 AYVAZIAN L F Friedlander s Bacillus Meningitis Successfully Treated with Streptomycin Consideration of Friedlander Bacillus Infections in Diabetes *Am J Med* 1948 V p 470
2 GRUBER S TURIN R D STERNBERG S D and RASCOFF H Friedlander s Pneumonia with Multiple Lung Abscesses Recovery Following Use of Streptomycin and Aureomycin *J Pediat*, 1950 XXXVI p 237
3 JACOB S S and TOP F H Friedlander Bacillus Meningitis 7 Cases with Recoveries (following Penicillin Streptomycin and Sulfadiazine Sulfonamide Therapy) *Ann Int Med*, 1949 XXVIII p 1003
4 LONG P H Clinical Use of Antibiotics *Med Clin No Amer*, March 1950 p 307

Tetanus

1 BOLES T C and SMITH J H Mephenesin in Treatment of Tetanus *Jour Amer Med Assoc*, 1951 CXLVI p 1296

GODMAN H F and ADRIANI J Management of Patients with Tetanus Some Clinical Experiences with Various Muscle Relaxing Agents *Jour Amer Med Assoc* 1949 CXLI p 754

3 WELD M R PURVIS D F and WARNKE R D D Tubocurarine in Wax and Oil for Control of Muscle Spasm in Tetanus *Jour Amer Med Assoc* 1948 CXXXVIII p 1087 1949 CXXXIX p 45

Anthrax

1 COLD H and BOGER W P Newer Antibiotics in the Treatment of Anthrax *N E J Med* 1951 CCXLIV, p 391

Glanders

1 Foreign letters (Turkey) Acute Glanders Responds to Streptomycin *Jour Amer Med Assoc* 1950 CXLII p 45

CHAPTER IX

DISEASES DUE TO ACID FAST BACILLI

Tuberculosis

Until recently the treatment of tuberculosis has been largely passive, with rest, diet, climate, et cetera being used as adjuvants to nature's efforts at healing by the reaction of normal adjacent tissues Now these methods of passivity still of great importance in treatment have had added to them the use of several chemotherapeutic and antibiotic substances and various surgical procedures Earlier recognition of the presence of tuberculous disease especially by x ray and accurate early specific identification of tubercle bacilli by newer methods, including cultural ones, have changed the kind of problems presented to the physician in his treatment of the patient with tuberculosis Still for most patients tuberculosis remains essentially a disease of long duration needing careful management for years especially if the possibility of its recurrence in the apparently healed patient is kept in mind, as it always should be This probable long continuance of tuberculosis should be recognized by the physician and understood by the patient, after it has been simply and frankly explained to him, if treatment is to be efficient and effective

In the present status of knowledge of the diagnosis including the recognition of almost minimal foci of tuberculosis and on the basis of the probable progression of tuberculous lesions patients with tuberculosis especially those with pulmonary tuberculosis may be grouped into (1) those who obviously require treatment, (2) those who obviously do not require treatment and (3) those who are of uncertain status and need a period of observation to determine their need for treatment All who give any evidence of activity of a tuberculous lesion are in group (1) and a plan of treatment should be instituted for them at

once In contrast are those whose tuberculous lesions appear quiescent or healed as judged by x ray examination and from whom no tubercle bacilli are being discharged They have no symptoms and appear to be healthy individuals they need no treatment, but periodic examinations including various laboratory examinations for evidences of activity are desirable Between these two groups come those individuals whose tuberculous lesions are not clearly and certainly inactive who may discharge tubercle bacilli at intervals and who have some evidence of ill health possibly caused by their tuberculous lesions These patients should be studied very thoroughly and restudied at short intervals to see whether any evidence of spread of lesion appears or whether tubercle bacilli can be found in discharges from them Final judgment about whether they are to be treated for tuberculosis should not be made in less than 6 months of continued or oft repeated observation including many days of recording temperature at least twice daily morning and afternoon both during rest periods and after physical activity

The patients who obviously require treatment may be said to have active tuberculosis In active tuberculosis there are general principles of treatment that apply whether the main lesions of tuberculosis are in the lungs the gastro intestinal tract the genito urinary system or elsewhere These general principles will be discussed in the paragraphs immediately following and later such modifications as are needed for the various local forms of tuberculosis will be considered

General Principles of Treatment of Active Tuberculosis

Rest Rest including local rest obtained by surgical measures remains a very important possibly the most important factor in the treatment of active tuberculosis Every patient with active tuberculosis whether activity of process is judged by physical signs and x ray examinations or by symptoms particularly fever and malaise should be put to bed at once and kept there for at least a few weeks of observation while subsequent forms of treatment are being planned For many patients complete bed rest should be maintained for months until there is clinical and x ray *evidence of quiescence of the tuberculous lesions Fever elevated* pulse rate increase in blood sedimentation rate lymphocytosis and malaise are prominent and important signs of continuing activity of tuberculous lesions

Bed rest for the patient with tuberculosis means 24 hours in bed, when possible with the bed placed to have free access to fresh air with protection of the patient from excess of cold or heat For the bed to be out of doors part of the day is desirable in temperate climates and often in cold climates when the patient s bed and body are protected adequately against cold Sunshine is desirable in cool and cold weather In hot weather some form of air conditioning of the room is highly desirable The patient who has difficulty in using a bedpan or urinal should be allowed to use, with the nurse s help a bedside commode

The best bed to use is the so called hospital bed fairly narrow, on rollers and with adjusting mechanism so that the patient may be easily changed from reclining to half reclining or sitting positions by the nurse, with no physical effort on his part To maintain such bed rest, *nursing care* is required preferably by a trained nurse or attendant nurse, at times an intelligent member of the family can carry on the needed nursing care, if the patient remains at home In the early period of the treatment of active tuberculosis hospitalization is desirable followed later by a sojourn in a sanitorium this facilitates the needed special examinations of the patient and has value in his training and the adjustment of his morale also it leads to very frequent visits by the patient s physician, which is actually a very important feature of the best possible management of active tuberculosis, obviously the physician should secure the confidence of the patient early and maintain it throughout his management of the patient s treatment

Bed rest, except for the very ill patient does not mean lying flat in bed When the patient is kept flat in bed he should be turned frequently encouraged to change the position of his legs and arms as often as every half hour, and other precautions should be taken as described in Chapter I to prevent phlebothrombosis and thrombophlebitis

Except for the acutely ill the patient with active tuberculosis should be allowed to assume with the nurse s help a propped up position in bed, especially at mealtimes If and when this develops fatigue as it will do sooner or later the patient should be returned to the flat in bed position for a period of rest When propped up in bed he should be allowed to read to play solitaire et cetera under careful observation by the nurse, who must stop these occupations if and when there is fatigue

Talking often proves fatiguing to tuberculosis patients especially those with pulmonary lesions and it may induce coughing and dyspnea Consequently talking by the patient should be curtailed This need emphasizes the importance in the rest regime for limitations on and care

ful selection of visitors Visitors that excite the patient and keep him talking should not be permitted to see him

Nursing attentions, including use of bedpan urinals, bathing and tidying up, changing clothing and bed linen feeding et cetera should be spaced to reduce fatigue to a minimum The intelligent nurse can get all of these things accomplished for the patient s increased comfort with minimum fatigue to the patient if she is always alert to notice evidences of fatigue and will stop what she is doing so that the patient may have a period of rest

The transition from such complete bed rest as has just been described is most important Before commencing it the physician should be very sure that most of the evidences of activity of the tuberculous process have greatly decreased or disappeared Those familiar with managing tuberculous patients acquire great skill in judging these changes It is not a question of time for individual patients vary greatly in the number of months needed to develop quiescence of tuberculous process When the physician believes the time has come for the particular patient to cease the regime of complete bed rest the physician should indicate what in creased activity is to be allowed and judge whether this increase has in any way reactivated the process or been unduly fatiguing If it has not, progression to more activity should be allowed i e longer periods of sitting up and gradual increase in moving about Most patients are greatly pleased when bathroom privileges become an early part of their permitted increase in physical activity

Usually the rest period as just outlined needs to be continued for at least two years for some considerably longer than this For patients with pulmonary tuberculosis therapeutic pneumothorax to be described and discussed in a separate section will often modify and shorten the patient s period of greatly restricted physical inactivity

Diet In the febrile period of active tuberculosis diet should be that appropriate to any acute infectious disease as described in Chapter I But since tuberculosis is for most patients a disease of long continuation the diet as early as is possible should be shifted progressively though grad ually in the direction of becoming a normal diet It should be balanced in proportion of protein carbohydrate and fat with adequate content of the essential vitamins and containing daily at least 60 to 75 gm of protein and 2500 to 4000 total calories depending on the sex and size of the patient and the degree of physical activity being permitted To accomplish this final goal may require a very long time for some patients since slow decrease in the activity of the tuberculous process often

retards progression from bed life to average physical activity, and with many patients nausea poor appetite, and diarrhea are present to restrict the kinds and amounts of food that can be given There is nothing in the disease tuberculosis to interdict the use of any particular food items except the preference of the patient his digestive capability and the need for a total of food items to make up a balanced diet with the calorie content indicated a few sentences back In other words a diet weighted in protein in carbohydrate or in fat is not needed

In the more active early stages of tuberculosis frequent feedings are desirable As the patient improves gradually shift to a three meal a day plan supplemented between meals by milk sweetened fruit juices and possibly egg nogs containing a jigger of whisky or rum remembering, however that the uncooked egg is not a very digestible food as contrasted with a cooked egg The latter fact contraindicates the effectiveness of raw eggs which were for so long diligently urged on the tuberculous patient

The fluid content of the diet including drinking water should be the average normal unless fever sweating vomiting diarrhea and/or dyspnea increase fluid loss from the body and make a need for increased fluid intake to prevent dehydration Not often is parenteral fluid needed by these patients The need for greater fluid intake can easily be judged from urine output which should not be less than 1500 to 2000 cc every 24 hours

Hospital or Sanatorium versus Home Treatment In the early phases of treating the patient quite ill to severely ill with tuberculosis, a sojourn in a general hospital is desirable In such a hospital there is easily accessible everything needed for completing an accurate diagnosis and for estimating the distribution and degree of activity of the tuberculous lesions factors so necessary to planning for the individual patient the form of treatment most likely to bring quiescence of activity of the tuberculous lesions as rapidly as possible In many well equipped sanatoria for tuberculous patients these facilities are present if so sanatorium treatment may be commenced without preliminary stay in a general hospital After this preliminary stay in a general hospital it is advisable to send the majority of the tuberculous patients with continuing evidence of activity of process to a sanatorium for the care of patients with tuberculosis and especially is this true for those with pulmonary tuberculosis Nowhere else can the patient learn so well how to guard against infecting others and how to take care of himself and develop the needed morale to meet the limitations imposed on him by his disease Contact with

other patients there helps greatly and of course nurses and physicians play a large part in this very necessary education of the patient education to prepare him for the day of his return to reasonably normal activities of life

It hardly seems necessary to mention that such a sanatorium ideally should be situated away from crowded city districts and have access to clean air and sunshine Experience has shown however that these conditions are not absolutely necessary the tuberculous patient can progress satisfactorily within the city and under home management if the ingenious nurse and physician will arrange the home for a rest cure with fresh air from ample windows improvised sleeping porches et cetera to imitate conditions found in the sanatorium Of course some homes in suburban residential districts small towns and the country have situations analogous to those of the sanatoria To carry out proper home care however is not easy and sanatorium care should be made available if that is possible instead of attempting to surmount the many inherent difficulties of proper home treatment Home treatments of course will lack those contacts with other patients so important to the person with tuberculosis contacts ideally provided by the sanatorium Home treatment may be necessary while awaiting access to a sanatorium If this happens then the home should be arranged even temporarily to imitate conditions found in the sanatorium

Climate Parts of the country with abundance of sunshine freedom from dampness moderate elevation average temperature range with few very hot days and infrequent sudden changes are ideal for sanatorium care of patients with tuberculosis Patients also do well in places with cold even very cold winter weather and in dry warm to hot desert regions with considerable elevation and cool nights Patients should be sent to such places provided they can afford it financially do not become lonely because of absence of family and friends do not have too long and uncomfortable transportation to the place are not homesick go under the care of a skilled physician et cetera — conditions which cannot be met by all patients nor found in every place

The patient with an active tuberculous process should never be just sent to a climate supposedly good for tuberculosis to live and probably work on his own without intelligent medical supervision This may be good however for the patient with a tuberculous lesion that has become quiescent who is now ready to lead a life of only moderate restriction Climate per se is less important than the many associated conditions needed in the treatment of tuberculosis This is shown by the variety

of climatic conditions in which successful sanatoria for the tuberculous are situated Change of scene and its stimulation are important factors in the benefit of climate

It is fair to say that in general today climate seems to be regarded as a rather minor item in the best care of the patient with tuberculosis and increasingly sanatoria for care of patients with tuberculosis are being less used many of them are seeking patients with diseases other than tuberculosis — children and young people who have had rheumatic fever and patients with chronic arthritis chronic Bright's disease, chronic heart disease arteriosclerosis or other chronic diseases The introduction of surgical measures into the treatment of tuberculosis is responsible in considerable part for these changes

Isolation Single-room isolation is highly desirable for patients with active tuberculosis during their stay in a general hospital or at home especially for those who have pulmonary lesions and are raising sputum containing tubercle bacilli Such isolation is desirable but not necessary in sanatoria limited to the care of patients with tuberculosis All excreta that may contain tubercle bacilli should be promptly and thoroughly disinfected or destroyed Dishes and other articles used in eating should be placed in boiling water or have steam sterilization as soon as they have been used All bed linen and washable garments of the patient nurses and physician should be put into bags at once after use and kept there until sterilized All in contact with the patient should wear sterilizable overgarments and head coverings as well as face masks if the patient coughs because of a pulmonary lesion Sputum should be spit into receptacles that can and will be burned anything used to wipe the mouth should be put at once into a paper bag and bag and contents subsequently burned The patient should be taught to cover his mouth and nose when coughing and never to cough toward the face of another person The properly trained patient who follows the directions just described can with care make himself of very little danger to family friends and any contacted individuals and so become very little of a menace in the spread of tuberculosis a spread which today is largely caused by careless individuals with open lung lesions who cough unguardedly Especially dangerous is the individual who does not know that he has tuberculosis some of these people daily cough out into the community literally myriads of tubercle bacilli

Psychotherapy In a disease like tuberculosis almost certain to be of long duration and to upset greatly the life of the patient in all of its aspects the reactions of the patient will need very careful consideration

and wise guidance The physician in charge should learn in great detail what sort of an individual his patient is and how he has lived and reacted before the development of tuberculosis His economic status must be understood and his family and social relations must be studied His worries must be understood and met Emotional tensions must be recognized and faced and solved with the patient The periods of depression inevitable to almost every patient with tuberculosis will need recognition with helpful guidance through them The morale of the patient must be maintained

The wise physician as a rule can handle all of these situations if he gives time to his patient and gains his confidence There must be frankness and complete honesty on the part of both physician and patient without them good results from treatment are unlikely For some patients the problems become so complex that the help of a psychiatrist will be needed but actually this happens infrequently possibly because the physician who cares for many patients with tuberculosis gradually becomes very skilled in the psychotherapy his tuberculous patient needs

Surgical Treatment Including Therapeutic Pneumothorax

Surgery has now become of great importance in the treatment of tuberculosis In some forms of the disease the surgeon plays as large a part in treatment as does the physician Therapeutic pneumothorax for convenience of discussion is included in this section on surgical treatment although it is a procedure carried out regularly by the physician who undertakes the treatment of pulmonary tuberculosis Because of its great value and consequently frequent use therapeutic pneumothorax will be discussed first

Therapeutic or Artificial Pneumothorax This method consists of introducing filtered air into the pleural space in measured amount under manometric control of intrapleural pressure Its object is to bring about collapse of the lung on the side of the pneumothorax in order to decrease its respiratory movements to slow circulation of blood and lymph in it and to approximate progressively the walls of any cavities present in the lung until in many patients cavities become very greatly decreased in size or even completely obliterated

To produce therapeutic pneumothorax special apparatus is needed This consists of a hollow needle or trochar with stilette arranged so that by tubing it can be connected with two bottles One bottle is filled with

water which, when the bottle is elevated, flows into the other, displacing air in the latter along the tubing through the needle or trochar into the pleural space Connected to the tubing is a manometer on which pressure of the introduced air can be read A series of valves with cocks are introduced in the tubing in different places to control air flow, allow pressure readings et cetera When the apparatus is ready, after skin sterilization the sterilized needle or trochar is pushed with aseptic precautions between two ribs into the pleural space, and air introduction is begun Filtered air is used These are the general principles of the apparatus for producing therapeutic pneumothorax, numerous types of apparatus with a variety of modifications are on the market

Often at the first sitting only a small amount of air can be introduced before the procedure must be stopped because of pain dyspnea, cough or signs of vasomotor collapse These same symptoms may follow subsequent refills After an interval of a day or two more air should be introduced, and this procedure should be repeated until considerable collapse of the lung has been brought about Then at longer intervals refills of air are to be made to maintain pulmonary collapse, in most patients pulmonary collapse must be maintained by pneumothorax for a period of 18 to 36 months after cavity closure conversion of sputum and relief of symptoms The degree of pneumothorax should be visualized by repeated x-rays and at the same time the lung should be examined for any change in the appearance of the tuberculous process

Intrapulmonary Pneumonolysis Pleural adhesions are often present These may so obliterate the potential pleural space that they prevent completely the production of pneumothorax, fortunately this is not a frequent occurrence On the other hand pleural adhesions do often hinder satisfactory collapse of the lung To obtain the latter it may be necessary to sever the adhesions by a galvanocautery or a diathermic current after localizing them by x ray This can be done through a canula under visualization through a thoracoscope, using the technic devised by Jacobaeus, this process is called intrapleural pneumonolysis

In order to secure satisfactory anatomical collapse it may be necessary to do pneumolysis in as many as 90 per cent of pneumothorax cases

Use of Therapeutic Pneumothorax In general it seems wise not to use therapeutic pneumothorax until a period of sanatorium rest treatment has been followed since many patients do surprisingly well under such management and because, once begun, therapeutic pneumothorax almost invariably must be maintained with repeated refills over long periods—several years for most patients By no means should therapeutic pneumo

thorax be regarded as a convenient short cut to the solution of the problem of treatment of pulmonary tuberculosis Actually it is one form of rest treatment and should always be used in connection with the other forms of rest and general management discussed in preceding sections For patients to whom it is suited it is a very valuable adjunct and for many of them expedites their progress toward the period of ambulation and less restricted activities of life

It is particularly useful when the active tuberculous lesion with cavitation *is on one side with no localized non progressive lesions on the* other side or only a small one Patients with more extensive lesions not doing well under simple rest management may be given pneumothorax and this often gives excellent results even when the tuberculous lesion in the other lung is fairly active Rarely should bilateral pneumothorax be tried In recent years there has been an increase in the use of pneumothorax in the treatment of patients who have pulmonary tuberculosis *with both slight and extensive cavitation and also even of patients who* have active unilateral pulmonary lesions without cavitation after increasingly shorter periods of sanatorium rest In general best results are obtained when pneumothorax is given to those patients with unilateral *lesions which on x ray examination show a light fluffy scattered lesion* Those with heavy dense or grossly confluent lesions usually do not give as satisfactory results The extent of the destruction as evidenced by cavity size degree of caseation amount of contraction fibrosis and obstruction is more important than cavity size alone in deciding whether pneumothorax or more extensive surgery should be used In general pneumothorax does not give good results in the presence of extensive disease

For the control of hemoptysis in cases with cavitation pneumothorax is usually effective When sputum is abundant and rich in tubercle bacilli as so often is true of patients with extensive cavitation pneumothorax since it causes collapse of the cavities greatly reduces sputum and decreases the number of bacilli being coughed up

When successful pneumothorax decreases fever and other toxic symptoms reduces sputum decreases the number of tubercle bacilli being coughed up and finally eliminates them and decreases the tendency of the tuberculous lesions to extend to other parts of the lung and to other places in the body These are the reasons for using pneumothorax and the criteria in addition to changes demonstrated by x ray by which the efficiency of pneumothorax is judged When these changes appear obviously pneumothorax should be continued by refills which maintain

collapse of the lung As time goes on, air is less rapidly absorbed from the pleural space and the time between refills can be increased from the early intervals of a few days to later intervals of a few weeks When to refill should be judged by x-ray examination and manometric measurements of intrapleural pressure

Various complications may follow therapeutic pneumothorax Serofibrinous pleurisy is a frequent one Empyema is a very occasional one and, though it occurs rarely may end in a pleuro bronchial fistula Air embolism is a rare complication Thickening with organization and fibrosis of the pleura may result and hinder re expansion, when the time comes to stop the refills, it may become a cause of ceasing the pneumothorax These complications may cause a shift to other forms of treatment in place of pneumothorax

It would seem wise for the physician who has not had extensive experience with the treatment of pulmonary tuberculosis to consult with one who has before making a pneumothorax since this is a situation in which clinical experience is of great value and for which set criteria of selection are very difficult to formulate

Length of Continuance of Therapeutic Pneumothorax No fixed rules about the length of time for continuing therapeutic pneumothorax can be given As long as the patient shows continued improvement, it certainly should be continued Some set disappearance of tubercle bacilli from the sputum as a very important criterion of ending the pneumothorax Others say continue until x ray shows complete collapse of all cavities However sometimes these changes do not take place and yet the patient s general condition is excellent now even for that patient discontinuance of pneumothorax is indicated In some patients after discontinuing refills re expansion of the lung fails to take place This situation may be allowed to continue but if complications develop then other surgical procedures are indicated such as thoracoplasty or possibly lobectomy or pneumonectomy

In general it may be said that once started continuance of therapeutic pneumothorax will probably be advisable for from 18 to 36 months after cavities have closed sputum has become free from bacilli and there is relief of symptoms Certainly no exercise should be permitted until 3 to 5 months after cavity closure and bed rest should be continued for at least 3 months after induction of pneumothorax The physician may decide that the time has come to end pneumothorax and take steps to that end However he may find that as re expansion of the lung goes on there develop evidences of reactivation of the tuberculous

process If so then refills should begin again and the pneumothorax be continued for a longer period The length of time for continuing pneumothorax is for many reasons a variable for each individual patient the physician must make numerous decisions These decisions can be based on some of the criteria already given in this discussion but clinical judgment based on previous experience must also have a large part in determining the physician s opinions about what to do and when Pneumothorax should be abandoned if there is evidence of increasing fluid formation or if the fluid shows evidence of bacterial infection or becomes purulent

Pneumothorax in Relation to Aviation The patient with an existing pneumothorax should be informed of the possibility that if he travels in an airplane that goes to high altitudes as is very usual at the present time the decreased atmospheric pressure may cause enough expansion of the air in the pleural cavity to produce discomfort even severe dyspnea and possibly serious consequences including hemoptysis This may be expected if the amount of air in the pleural cavity is large in amount and under considerable pressure Consequently the danger is greatest soon after air has been introduced The patient with pneumothorax will do well to consult his physician before undertaking an airplane flight The physician should remember that at times abrupt increases in elevation become necessary to avoid thunderstorms or other potential dangers even when the flight is presumed to be at only moderate elevation Flights in planes in which air pressure in the plane is increased as atmospheric pressure decreases present no danger to the individual with a pneumothorax unless the mechanism to adjust pressure fails to work Many airplanes now fly at high altitudes with air pressure within the plane regulated to prevent its drop when atmospheric pressure decreases

Phrenic Nerve Paralysis

Complete paralysis of the phrenic nerve on one side will cause paralysis of the diaphragm on the same side and decrease respiratory motion in so far as it is contributed to by diaphragmatic movements thus giving considerable rest to the lung on that side Also the paralyzed diaphragm remains in an elevated position adding a factor of partial pulmonary collapse Phrenic nerve paralysis has been utilized to a considerable extent in the treatment of pulmonary tuberculosis in the same way and for the same conditions as discussed under Therapeutic or Artificial Pneumo-

thorax It has seemed particularly useful as a means of controlling hemoptysis

Less effective than pneumothorax, it may be used to indicate whether the latter will prove helpful if some benefit follows phrenic nerve paralysis then pneumothorax can be instituted Phrenic nerve paralysis has the advantage that, if produced by nerve crushing, it will be of only 4 to 6 months duration, because the nerve in that time will regenerate and diaphragmatic movements will return If continuation of the effect is desired, the phrenic nerve can be crushed again For this reason crushing has an advantage over excision of the phrenic nerve Some prefer alcohol injections of the phrenic nerve Phrenic nerve paralysis will not cause so complete pulmonary collapse as follows therapeutic pneumothorax with repeated refills, therefore it cannot be expected to accomplish as much as the latter when the tuberculous lesion is extensive with large cavities For probable success it should be used only when cavities are 3 cm or less in diameter or when combined with surgical procedures where a small section or a lobe of the lung is removed If cases unsuited to the treatment undergo phrenic nerve paralysis good results should not be expected Failure to obtain complete paralysis of the diaphragm because not all accessory branches have been blocked is another reason for poor results from this form of treatment If other nerves in the neck are injured during the operation then poorer results may be expected also In some clinics this operation is used quite extensively while in other clinics it is rarely used at present

Pneumoperitoneum

The introduction of filtered air into the peritoneal cavity with repeated refills will elevate the diaphragm on both sides and decrease its respiratory excursions This will decrease pulmonary expansion with each inspiration and contribute an element of rest Its pulmonary effect is bilateral, which may be of importance in certain selected cases Also it has been used with unilateral phrenic nerve paralysis to increase the effect of that treatment It can be used to obtain some improvement as a preliminary to more extensive surgical procedures or in conjunction with surgical procedures on the lung

Abdominal Binder

Some physicians use a type of abdominal binder as a substitute for pneumoperitoneum in patients with phrenic nerve paralysis The binder

is to compress the upper part of the abdomen and crowd the diaphragm up and decrease the amplitude of its respiratory movements

Extrapleural Thoracoplasty

This is a collapse therapy procedure to be used when other less extensive procedures have failed and as a primary collapse procedure for patients having strong pleural adhesions or far advanced tuberculosis with large apparently thick walled cavities The collapse from extrapleural thoracoplasty is produced in that part of the lung over which ribs have been removed The treatment is particularly suited to patients with lesions in the upper third or half of the lung Removal of 6 or 7 ribs in stages is the procedure now generally advised This is not a suitable place for discussion of the various forms of surgical technique appropriate to different patients However extrapleural thoracoplasty is a valuable form of treatment in advanced pulmonary tuberculosis such patients should be referred by the internist to surgeons skilled in the technique of pulmonary surgery and with clinical experience in the problems of advanced chronic pulmonary tuberculosis

Lobectomy, Pneumonectomy, and Wedge Resection

In recent years lobectomy pneumonectomy and more recently wedge resection have been utilized increasingly on patients with pulmonary tuberculosis The surgeon can contribute important means of treating certain types of advanced pulmonary tuberculosis by the skilful performance of these operations Some clinics now advise them for some patients instead of extensive thoracoplasty During the last 5 years *the combined operation of upper lobe removal and thoracoplasty of the first 4 or 5 ribs* or lower lobe removal combined with temporary paralysis of the homolateral portion of the diaphragm has grown in favor These procedures are less mutilating and there is retention of more pulmonary function Patients will accept this surgery when other forms such as extensive thoracoplasty may be refused These procedures will not however be of more benefit than carefully performed thoracoplasty *except possibly in cases of lesions of the lower lobe All surgical* procedures should be combined with chemotherapy since the sensitivity of the organism to chemotherapeutic agents has greatly increased the patient s ability to undergo surgery and has greatly improved the prognosis The recent trend is to secure as much resolution of the reversible aspects of the disease as possible by bed rest chemotherapy pneu

mothorax pneumoperitoneum, and so forth and thus reduce the extent of surgical resection and submit the patient to surgery at the most favorable time When this is done, complications are low and not infrequently a much smaller 'wedge resection' can be substituted for a lobectomy with equally good results

Other Surgical Procedures

In addition to the surgical procedures already described there are a number of others to be used for special purposes Among these are oleothorax in which in special circumstances oil instead of air is introduced into walled off pleural spaces extrapleural pneumothorax, extrapleural pneumonolysis with paraffin gauze or other filling, scaleniotomy, scaleniectomy intercostal nerve paralysis Monaldi cavity drainage, open cavity drainage et cetera At times one or the other of these procedures may be of some use but for the most part they have been abandoned

Diagnostic and Therapeutic Bronchoscopy

Bronchoscopy is being used more and more in the study and treatment of pulmonary tuberculosis along with other medical and surgical techniques In the beginning regarded as hazardous in pulmonary tuberculosis now, in the hands of a skilled bronchoscopist it has but little danger for the tuberculous patient By bronchoscopy stenosing lesions of the bronchi and ulcerative lesions of bronchi and trachea can be recognized and treated and this in many patients will add a very beneficial feature to other therapeutic procedures being used It is very valuable in the treatment of patients with tuberculous tracheobronchitis or bronchitis

Chemotherapy and Antibiotic Therapy

As in all other infectious diseases for the treatment of tuberculosis to become satisfactorily effective the great need has been for chemotherapeutic or antibiotic agents which while being bacteriostatic and/or bactericidal for tubercle bacilli in vitro would be similarly effective in vivo without being more than mildly toxic for their hosts including man Although this goal has not been reached for tuberculosis as satisfactorily as for numerous other bacterially caused infectious diseases great progress has been made in recent years there are now chemotherapeutic and antibiotic agents that have been shown clinically to have a definite therapeutic value in various types of tuberculosis nothwithstanding the

many inherent qualities of the disease that make it especially difficult to obtain in man an adequate bacteriostatic and bactericidal effect on the tubercle bacillus It does not seem necessary in this discussion to elaborate on the latter they are known to all who have struggled to cure patients with tuberculosis

Chemotherapeutic Agents Of these the sulfones have been found to be effective in experimental tuberculous infections of animals and clinical reports indicate some value from them in treating tuberculosis in man Of the sulfones four — glucosulfone sodium (Promin) sulfoxone sodium (Diasone) thiazolesulfone (Promizole) and tetrasulfone (Sulfetrone) — have been studied particularly in both tuberculosis and leprosy with clinical reports of improvement from them in both diseases Reports on leprosy indicate that these drugs can be used in man over long periods of time 3 to 6 years with considerable safety This indicates that they can be used similarly with safety in patients with tuberculosis and already there are a few clinical reports of such cases Besides the sulfones of which 59 compounds have already been investigated other chemicals have also been found to affect the tubercle bacillus and are being studied Among these are the glycerite of hydrogen peroxide the sodium formaldehyde bisulfite derivative of 5 amino 2 butoxypyridine para aminosalicylic acid and the thiosemicarbazones

From these many investigations should eventually come chemotherapeutic agents which will be of much value in treating tuberculosis Of the chemotherapeutic agents mentioned above Promin and Promizole seem to have been tried most often and especially in leprosy have they been given daily over long periods of time with benefit and no bad effects Promin is used most satisfactorily by a parenteral route while sulfoxone (Diasone) and thiazolesulfone (Promizole) are satisfactorily administered by mouth The intramuscular or intravenous dosage of Promin is 1 to 2 gm daily The recommended mouth dosage of Diasone begins with 1 tablet of 0 3 gm daily increased gradually to 3 such tablets a day the mouth dosage of Promizole should be 1 tablet of 0 5 gm or 1 gm daily gradually increased to 6 to 8 gm daily With all of these rest periods from the drug from time to time have been advised Toxic effects have been few the sulfones do not cause crystalluria or hematuria as do the sulfonamides

When given in the dosage just described especially in conjunction with streptomycin the sulfones have some slight therapeutic value in various forms of tuberculosis However there has not been a sufficient number of patients so treated in comparison to controls without chemo

therapy to justify definite statement about daily dosage length of treatment, or clinical results

Para-aminosalicylic acid (Pamsyl) This chemotherapeutic agent, although not as effective against the tuberculosis organism as streptomycin, has a definite place in the treatment of the disease It supplements the action of streptomycin and prolongs the period before streptomycin resistance develops It may be used alone if so desired but best results are secured when it is used concurrently with streptomycin A dose of 3 0 gm of the sodium salt 5 times a day is recommended Severe dermatoses may occur and gastro intestinal irritation, nausea vomiting, and diarrhea are sometimes encountered Occasionally these may be of sufficient severity to warrant discontinuing the drug The gastro-intestinal symptoms are relieved somewhat by antacid therapy with aluminum hydroxide gel

Thiosemicarbazones These interesting compounds apparently have some ameliorative effect in tuberculosis There is not yet sufficient experience with them properly to evaluate their status in therapy Iso nicotinic acid hydrazide (Rimifon Marsilid, Dinacrin, Nydrazid), in a dose of 2 to 4 mg per kilogram of body weight daily, has recently shown definite promise Earlier reports were too enthusiastic but sufficient experience with the drug now indicates that it may be as useful as para aminosalicylic acid as adjunctive treatment with streptomycin Organism resistance develops in a fairly high percentage of cases and clinical relapses occur when the drug is used alone Appetite seems to be definitely stimulated and patients have a sense of well being X ray and clinical evidence of healing is slow in appearing and in some patients no real improvement is seen As yet it is too early to assign this agent a definite place in the therapy of tuberculosis Perhaps it is best used in conjunction with streptomycin Isonicotinic hydrazide passes readily into the spinal fluid and this fact may make it especially valuable in the treatment of tuberculous meningitis

Antibiotic Agents Penicillin has been found non effective against tubercle bacilli, while streptomycin has been demonstrated to be an antibiotic agent definitely effective in action on the tubercle bacillus in both animals and man Streptomycin has certain toxic effects as described earlier (see p 25) which need to be watched for but they are not often serious enough to prevent the therapeutic use of streptomycin in human tuberculosis Dihydrostreptomycin can be used if toxic or allergic effects do appear when streptomycin is being used

However the tendency for patients to develop streptomycin resist-

ant tubercle bacilli as the use of streptomycin is continued is a serious drawback for it may lead to reactivation of the tuberculous process in patients after a period of streptomycin produced improvement How to meet this defect in streptomycin treatment is a very important problem for investigation It points to the great need for other antibiotics effective against the tubercle bacillus which can replace streptomycin when streptomycin resistance develops Until such are found the best that can be accomplished is to push streptomycin therapy vigorously Even though streptomycin resistant organisms develop many observers find that improvement continues if the streptomycin para aminosalicylate therapy is continued several months Some patients will have their tuberculous process arrested before streptomycin resistance develops this has happened for example in some of the patients with tuberculous meningitis treated intravenously and intrathecally with streptomycin

The dosage of streptomycin which gives good results with minimum toxicity is 1 0 to 0 gm intramuscularly given every 3 days or twice a week The lower dosage is recommended for patients weighing less than 1-0 pounds Intrathecally the dose has been 0 2 gm daily

In the very acute early forms of tuberculosis such as tuberculous meningitis and generalized miliary tuberculosis, streptomycin is valuable and should be given in 2 0 gm doses every third day along with 30 to 40 gm of para aminosalicylic acid daily As these forms of tuberculosis are otherwise almost invariably and rapidly fatal streptomycin should be used in their treatment Its use in extrapulmonary tuberculosis such as lesions of the mucous membranes respiratory tract gastro-intestinal tract draining cutaneous sinuses peritonitis bone and joint tuberculosis genito-urinary tract lesions and tuberculosis of the eye ear and pericardium is recommended as all have shown favorable responses to streptomycin therapy

Combined Chemotherapeutic and Antibiotic Agents Combining streptomycin therapy with para aminosalicylic acid gives better results and there is less tendency for streptomycin fastness to develop Streptomycin given in conjunction with Promizole may also have value

Steroid Hormones The status of corticotropin or cortisone in the treatment of tuberculosis is not yet established In the exeprimental tuberculous animal they seem to do more harm than good For the present their use is not recommended for the treatment of tuberculosis in man

TREATMENT OF DIFFERENT FORMS OF TUBERCULOSIS AND OF THEIR SPECIAL SYMPTOMS

Pulmonary Tuberculosis

All that has been stated under General Principles of Treatment of Active Tuberculosis should be applied in the treatment of patients with pulmonary tuberculosis As a rule these patients present themselves in the stage needing bed rest, but not many of them should be flat in bed throughout the day and night Some, on account of cough and dyspnea do best in a propped up or semi sitting posture in bed through the day and night while others are comfortable flat in bed for day rest periods and for sleeping at night, but for other periods are more comfortable propped up in bed Some very ill patients are most comfortable out of bed sitting up supported by pillows in a large chair

The most important aspect of *isolation* of the patient with pulmonary tuberculosis is the protection of others from air borne tubercle bacilli and their droplet dissemination after the patient has coughed Direct contact with tubercle bacilli in the air about the patient is a primary means of spreading tuberculosis Also air borne tubercle bacilli may get into food or alighting on various objects including the floor, may be carried by finger contacts or in dust to non infected individuals Sputum and all that comes in contact with it should be destroyed promptly Every patient must be trained carefully in the care of his sputum before discharge from the sanatorium certainly before his contacts with others increase much beyond those with his physician his nurse, a few members of the family, and an occasional visitor all of whom can be expected to guard themselves against infection

Special Symptoms of Pulmonary Tuberculosis Hemoptysis This if very slight requires no special treatment With larger hemoptyses, and particularly with very large ones the patient should be given complete bed rest preferably propped up in bed and be positively reassured by the physician that the bleeding will subside as it almost surely will do except in the case of massive hemorrhage from a large artery eroded as it crosses a cavity Cough should be discouraged codeine phosphate 30 to 60 mg should be given promptly in a hypodermic dose Codeine is preferable to morphine or methadone, if codeine is not effective morphine sulfate 8 to 10 mg or methadone 5 to 10 mg may be given hypodermically Too great sedation should be avoided as it unduly depresses desirable reflexes If hemoptyses continue therapeutic pneumothorax on the side of greatest cavitation is advisable With persistant

bleeding small transfusions of blood 100 to 300 cc, are advisable If the patient goes into shock, he should be kept warm and given transfusions of whole blood or plasma If there have been repeated hemoptyses even small ones artificial pneumothorax should probably be instituted if the active lesion is unilateral as it usually is

In patients with or without therapeutic pneumothorax aviation at the higher altitudes may prove conducive to hemoptysis Consequently patients with pulmonary tuberculosis and evidence of a ready tendency to hemoptyses should be warned against high flying except in airplanes in which inside atmospheric pressure will be increased to offset the outside rarified atmosphere of high altitudes

Cough and Expectoration So often an integral part of pulmonary tuberculosis the general measures already outlined for the treatment of active tuberculosis are important for decreasing cough and expectoration The presence of cavitation or bronchiectasis is the cause of abundant expectoration which is desirable for their drainage Patients should be encouraged to raise as much sputum as possible in the morning on awakening or following breakfast change of position with coughing will often accomplish this postural drainage may be very effective After this there should be only occasional expectoration and little cough the patient can and should train himself to restrict coughing by avoiding those acts which start it

If there is continued coughing tuberculosis of the larynx is a possible cause Laryngoscopic examination will show it if present If found it should have appropriate treatment to be described in a later section In some patients tuberculous tracheal or bronchial lesions cause the continued coughing They can be diagnosed by the bronchoscope If present they should receive local treatment through the bronchoscope

Dry irritative cough sometimes present will be decreased by steam inhalations medicated with menthol benzoin or gomenol Dihydrocodeinone (Hycodan) bitartrate 5 to 15 mg by mouth 3 or 4 times in 24 hours may be effective when other remedies fail to relieve the cough Sedative inhalations also are often helpful the compound being dropped on gauze to be held over nose and mouth while inspiring For this the following is an example

Menthol	15 cc
Spirits of chloroform	30 cc
Oil of eucalyptus	60 cc

If sputum is tenacious or hard to raise, some one of the following mixtures containing ammonium chloride should be given

Rx	Ammonium chloride	15 0 gm
	Codeine phosphate	0 4 gm
	Syrup of citric acid	60 0 cc
	Distilled water to make	120 0 cc
Sig	1 teaspoonful every 3 hours	

Rx	Ammonium chloride	15 gm
	Compound mixture of glycyrrhiza	90 cc
Sig	1 teaspoonful in ¼ glass of water every 3 hours	

Rx	Ammonium chloride	30 gm
	Tincture of hyoscyamus	30 cc
	Compound syrup of squills	30 cc
	Chloroform water	120 cc
Sig	1 teaspoonful every 3 hours in ¼ glass of water	

Often these preparations will cause the production of a more liquid less tenacious sputum more easily raised and so lessen coughing With persisting abundant sputum and cough collapse therapy of some type, as already described is indicated Therapeutic pneumothorax is preferable for most of these patients unless pleural adhesions restrict or prevent its effectiveness in which event other surgical measures would be indicated

Pain is usually caused by pleurisy and can often be controlled by using a well adjusted chest binder made of firm cloth padded with a layer of cotton and having straps with buckles so that it can be adjusted tightly around the chest and kept in this adjustment by periodically tightening the straps Adhesive strapping of the chest may be used instead of the binder but usually this is not so satisfactory Codeine phosphate in repeated hypodermic doses of 15 to 30 mg or dihydrocodienone (Hycodan) bitartrate 5 to 15 gm given orally may prove useful in lessening pain if not effective morphine sulfate 8 mg or methadone 5 to 10 mg should be substituted Care must be taken to avoid addiction, especially when morphine is used for this purpose

Fever and Sweating Along with general measures for the treatment of active tuberculosis cool baths and alcohol rubs are helpful Antipyretic drugs are seldom advisable Atropin may be given for sweating

but unless it is used in large amounts as a rule it has very little effect with large doses dry mouth and tachycardia usually result making the necessary dosage undesirable or actually harmful If there is cavitation failure of the cavities to drain as shown by x ray may be the important causative factor of fever and sweating if this is true bronchoscopic drainage or therapeutic pneumothorax is indicated

For most patients fever and sweating decline rapidly as a result of the various general measures already described and no special treatment is needed

Dyspnea and Cyanosis Moderate dyspnea is to be expected when there is fairly extensive involvement of lung parenchyma by tuberculous lesions this dyspnea will increase as pulmonary involvement extends or if bronchitis or bronchial obstruction develops If the dyspnea from such causes is severe enough to disturb the patient oxygen inhalation should be added to the plan of treatment Especially is oxygen indicated when dyspnea is accompanied by cyanosis Dyspnea with or without cyanosis may be due to a coincidental cardiac insufficiency caused by any form of heart disease *If cardiac dyspnea is present* and this should be obvious from study of the patient appropriate cardiac therapy should be applied

When dyspnea develops rapidly it is often caused by pleural effusion as can be determined speedily by physical and x ray examinations Such dyspnea should be treated by thoracocentesis If it develops even more rapidly and its inception is especially abrupt pneumothorax is probably the cause This can be detected by physical examination and more readily by x ray study If present and severe this dyspnea should be relieved at once by needle puncture to allow the air under pressure to escape from the pleural space for this the usual thoracocentesis apparatus should be used and the air be allowed to escape through water partly filling the bottle that is in tube circuit with the needle

Generalized Lymphohematogenous Tuberculosis Including Acute Miliary Tuberculosis

The chronic forms of this disease need only general methods of treatment already outlined or no treatment at all The latter applies to scattered lesions which under observation by x ray or other methods appear to be inactive and remain so with no definite symptoms attributable to them *In acute forms especially generalized miliary tuberculosis* streptomycin 2 gm every 3 days and para aminosalicylic acid (Pamisyl sodium) 30 to 40 gm daily should be begun at once with the patient

receiving in addition general measures of treatment appropriate for a patient severely ill with any acute infectious disease Before the advent of streptomycin practically all of these patients died, now with streptomycin and para aminosalicylic acid, recovery is a possibility

Tuberculosis of Lymph Nodes

This form of tuberculosis has a strong tendency to heal, the healing should be stimulated by conservative therapy of bed rest, good hygiene, and nutritious diet General heliotherapy beginning with small doses and gradually increased is of value in the treatment of lymph node tuberculosis Streptomycin and para-aminosalicylic acid give good results in these cases Surgical treatment of accessible lymph nodes should be carried out when other measures do not give satisfactory results It is wise however, to be slow to resort to surgical treatment because, so often satisfactory healing without surgery eventuates Not infrequently tuberculous lymph nodes softening and breaking down form discharging sinuses these may require special treatment, including surgical free drainage and excision to bring about their healing

Tuberculosis of Serous Membranes

When tuberculosis of a serous membrane causes enough serofibrinous exudate to produce pressure symptoms this fluid should be removed by appropriate drainage procedures This applies especially to the pleura and pericardium less so to the peritoneum With peritoneal tuberculosis, to open the abdomen surgically and then close it at once sometimes gives excellent results All of these patients should also be receiving a general rest dietary and antibiotic chemotherapy regime For some patients, especially those with peritoneal tuberculosis heliotherapy is of value If study of the fluid removed by tapping indicates an active tuberculous lesion streptomycin and para-aminosalicylic acid should be given as described for tuberculous meningitis such activity of lesion is indicated by the presence in the fluid of many polymorphonuclear leucocytes red blood cells, and tubercle bacilli

With less active tuberculosis of serous membranes which is far more common than the form just described there are adhesions of various types and extent Those in the pleura or pericardium need no special treatment unless as already described they hinder satisfactory pulmonary compression from therapeutic pneumothorax and need to be severed intrapleurally As for other forms of tuberculosis however,

these patients should have general rest and dietary and hygienic treatment Tuberculosis adhesions in the peritoneum may cause intestinal obstruction requiring immediate operation Such adhesions in the pericardium usually cause no symptoms and require no treatment

Chronic proliferative tuberculosis of the pleura often causes no symptoms and remains undetected until pneumothorax is attempted and fails to be effective When this happens some other form of surgical treatment of the accompanying pulmonary tuberculosis will be needed

Chronic proliferative tuberculous lesions of the pericardium may result in chronic constrictive pericarditis and require surgical removal to restore cardiac sufficiency It is this form of pericardial lesion that is so often associated with ascites of cardiocirculatory failure mechanism

Tuberculosis of Bronchi and Trachea

If tuberculosis develops in a larger bronchus as it frequently does obstruction may result This will prevent drainage from any cavity connected with it Even when there is no such cavity connection obstruction to a bronchus will probably lead to local suppurative processes In the tuberculous trachea ulcerations may develop Together these lesions are spoken of as tuberculous tracheobronchitis In either bronchus or trachea the ulcerations may bleed with resultant hemoptysis often they are a source of the continued presence of tubercle bacilli in the sputum when tuberculous parenchymal lesions are receding and cavities are undergoing collapse following therapeutic pneumothorax Treatment of tuberculosis of bronchi and trachea should consist of the general measures already described and streptomycin with para aminosalicylic acid Streptomycin aerosol therapy may be useful in these cases

Tuberculosis of Larynx

Laryngitis acute or chronic from tuberculous lesions localized in the larynx is of frequent occurrence most often associated with chronic pulmonary tuberculosis It should be suspected from a local tickling sensation from hoarseness and from pain on swallowing or coughing Any of these are indications for laryngoscopic examination If this reveals tuberculosis lesions in the larynx to the usual general measures of treatment should be added vocal rest and local applications to and/or cauterization of the tuberculous lesion under visual guidance by the laryngoscope Streptomycin and para aminosalicylic acid therapy are recommended Local applications of streptomycin and streptomycin aer

osol therapy are also of value Pain should be relieved by spraying with a 2 to 4 per cent solution of cocaine hydrochloride, a 2 per cent solution of tetracaine (Pontocaine) hydrochloride or a 2 to 5 per cent solution of tutocaine hydrochloride If pain is very severe, alcohol injection or excision of the superior laryngeal nerve may be necessary

Tuberculosis of Tonsils, Pharynx, Tongue, Lips and Nose

Local tuberculous lesions in these structures should receive local applications or electro cauterization Some of them, especially those of the tongue, should be excised, when tonsils are involved, tonsillectomy is often desirable Heliotherapy, applied locally with a quartz rod, may be useful in treating many of these Streptomycin is definitely helpful, as is para aminosalicylic acid

Tuberculosis of the Intestines

Usually but not always ulcerative lesions in the intestine due to tuberculosis develop in patients who are suffering from pulmonary tuberculosis with sputum rich in tubercle bacilli Consequently treatment needs to be part of the general therapeutic measures advised In general, modification will be needed in the diet usually taken by these patients the bulk should be reduced and food items leaving a large residue during the process of digestion omitted Very often a most important modification should be omission or great reduction in the amount of milk large quantities of which are ordinarily taken by tuberculous patients As soon as the diarrheal condition improves, the diet while remaining composed of low residue items should be increased gradually in calorie value and in protein content with adequate vitamins

Since symptoms will vary with localization of the tuberculous lesions, whether chiefly in the ileum colon sigmoid or rectum or very generally distributed symptomatic treatment should vary If there is diarrhea with or without abdominal pain and tenesmus the treatment should be essentially that already described for chronic ulcerative colitis With very severe diarrhea the amount of food will need to be greatly reduced and to be of low-residue kind certainly for a few days until the diarrhea lessens In these patients the use of tincture of opium [laudanum] or the camphorated tincture of opium (Paregoric) is very useful as is an evening cleansing enema of warm normal saline solution Colonic irrigations are not advised Streptomycin and para aminosalicylic acid

(Pamisyl) are useful and should be given So-called intestinal antiseptics whether given by mouth or in colonic irrigations should not be used Antispasmodic drugs seem too ineffectual to justify using them

Treatment by exposure of the abdomen to sunshine or to rays from infra red lamps of different sorts is a valuable adjunct to treating intestinal tuberculosis discharging sinuses if they have developed should be drained The latter often heal surprisingly rapidly under such treatment

If perforation of the intestinal wall with the development of peritonitis occurs or if intestinal obstruction develops surgical measures will be needed Penicillin aureomycin and streptomycin should be given in full dosage and surgical repair of the perforation made promptly

In an occasional patient intestinal ulcerative tuberculosis exists in the absence of pulmonary lesions or in the presence of very slight ones Usually the infecting organism in these patients is of the bovine type and the disease has been acquired by drinking raw milk from tuberculous cows With the very general elimination of tuberculous cows from herds and with the almost universal practice of pasteurization this form of tuberculosis has almost disappeared If it occurs it should be treated as described in the preceding paragraphs

If the hyperplastic form of tuberculosis develops in the intestine and is diagnosed the treatment should be surgical with probable excision of the involved loops of the intestine Hyperplastic tuberculosis is more frequent in the cecum and adjacent parts of the ileum and colon than elsewhere in the intestinal tract

Tuberculous lesions in the rectum and lower sigmoid are accessible to local therapy through the anoscope or proctoscope and should receive this form of treatment A perirectal abscess, if it develops should be drained surgically

Tuberculosis of the Urinary Tract

When there is a tuberculous lesion localized at any point in the urinary tract the patient should be treated with all of the general measures for tuberculosis In addition much of the treatment described for cystitis ureteritis pyelitis et cetera on page 613 should be applied Streptomycin with para aminosalicylic acid should be given

Since tuberculosis of the urinary tract is very often complicated by inflammation caused by bacteria other than tubercle bacilli antibiotics

effective against them should be used With tuberculous lesions present in the bladder, local treatment of focal lesions should be carried out through the cystoscope even though there is evidence of tuberculous lesions higher up in the urinary tract

When tuberculous lesion in the kidney is extensive and particularly when the involvement is dominantly unilateral, the tuberculous kidney should be removed even if there are also tuberculous lesions at lower levels of the urinary tract since often the latter improve following unilateral nephrectomy Nephrectomy is especially indicated when one kidney with tuberculous lesions has a very low degree of function In some patients one kidney will be almost destroyed by tuberculosis and its function is almost nil obviously such a kidney should be removed unless total renal function is so low that any operation is contraindicated

Calculi often complicate tuberculosis of the kidney or bladder Their removel is usually a desirable part of the treatment of tuberculosis of the urinary tract

From what has been said it is obvious that a genito urinary surgeon is a necessary adjunct to the study and treatment of tuberculosis of the urinary tract

Tuberculosis of Central Nervous System

Tuberculous Meningitis The most important and the most frequently occurring tuberculous lesion of the central nervous system is tuberculous meningitis The patient should have at once the regime suitable to any acute infectious disease of great severity and in addition streptomycin intramuscularly or intravenously and intrathecally The dosage for the former should be 1 to 2 gm of streptomycin every 24 hours divided into 6 or 8 doses and for the latter a total of 0 1 to 0 2 gm per 24 hours, both dissolved in sterile water which is injected into the spinal canal through the lumbar puncture needle after as much fluid as possible has been drained off For most patients lumbar puncture with drainage and subsequent injection of streptomycin should be performed daily or every other day depending on presence of pressure symptoms and toxic effects from streptomycin These treatments need to be continued for many days Intrathecal streptomycin may cause ataxia nystagmus, transient strabismus and vomiting when these occur longer intervals between intrathecal treatments become necessary

In addition to streptomycin para aminosalicylic acid is advised, as

better results are obtained from the combination than from streptomycin alone The dose of para aminosalicylic acid (Pamisyl sodium) is 30 to 40 gm, divided into 5 doses daily The use of Promizole 1 to 2 gm per day by mouth given in conjunction with streptomycin is helpful Isonicotinic acid hydrazide 4 to 10 mg per kilogram of body weight may also be helpful As yet there is insufficient data to indicate the place of this drug in the therapy of tuberculous meningitis The fact that it appears readily in the cerebrospinal fluid may enhance its value

Tuberculoma A far more infrequent tuberculous lesion of the central nervous system than meningitis is a tuberculoma which may develop almost anywhere in the cerebrum cerebellum or spinal cord It may be symptomless or cause symptoms from replacement of normal tissue or from pressure much as do neoplasms Before surgical exploration it is often diagnosed as neoplasm If there are symptoms surgical exploration with probable excision is indicated

Tuberculosis of the Adrenals

Tuberculosis of the adrenals either is symptomless or causes Addison s disease It requires no special form of treatment so far as the tuberculous lesion is concerned If Addison s disease develops it is to be treated as described under that heading

Tuberculosis of Other Tissues and Organs

Tuberculosis in any of its forms may and often does involve other tissues and structures than those described in the preceding pages Their treatment should be the application of what has already been described modified to fit local conditions

Pleural Effusion

It has been held by many that pleural effusion occurring in the presence of pulmonary tuberculosis should not be removed but should be left in place as it is 'nature s method of putting the involved lung at rest Contrary to this it has been our practice to remove promptly and slowly by thoracocentesis such collections of fluid and this has proved

beneficial with few recurrences when all fluid was removed It is our belief that all of the fluid that can be removed should be taken off, unless cough or pleural shock supervenes as an indication for ceasing removal of fluid At a later period the remaining fluid should be removed Except for occasional pain, when inflamed pleural surfaces come into apposition the patient usually becomes more comfortable at once If pain occurs it can be relieved readily by a binder or 30 mg of codeine phosphate By tapping as a rule dyspnea is relieved cough diminishes, and most important, a temperature that has previously been high will fall to normal, or nearly normal, and remain so In our experience such a procedure does not in any way hinder the later institution of pneumothorax therapy intrapleural adhesions do not seem to be promoted by such removal of fluid Furthermore follow-up studies of such cases have shown no increase or spread in the pulmonary process in fact the regressive response expected under bed rest and good supportive care takes place

After the removal of as much fluid as possible the patient should be sent immediately for stereoscopic films of the chest so that the nature and extent of the pathological process in the lung which may previously have been obscured by the fluid may be discerned

When thoracentesis is carried out for pleural effusion it seems to serve no useful purpose to introduce routinely air into the pleural space It may lessen pleural friction pain in some cases, which advantage certainly is offset by the confusing picture such a procedure usually gives on the roentgen film

Prophylaxis

Prophylaxis should be regarded as an important consideration in the management of patients with tuberculosis Certainly treatment cannot be said to be satisfactorily and completely carried out unless in addition to amelioration of the symptoms and cure of the activity of the lesions the spread of tuberculosis to others is being prevented Every physician who encounters a patient with tuberculosis whether or not he undertakes direction of the treatment is obligated to direct its prophylaxis

In final analysis prophylaxis in tuberculosis is concerned with (1) preventing the patient who has tuberculosis from spreading it to others and (2) preventing non tuberculous patients from acquiring the disease by direct or indirect contact with tuberculous patients To accomplish

these things is a problem of both public and individual health of groups and of individuals of public agencies and of individual physicians the latter co operating with the former In all of this the recognition of the presence of tuberculosis in the individual as early as is possible is of the very greatest importance Without early diagnosis the tuberculous patient cannot be taught how to prevent himself from being a danger to others How this is to be done has been discussed already in the section on Isolation in Chapter I

The early diagnosis of pulmonary tuberculosis which is the form of the disease most responsible for its spread from man to man by x ray examination of the chests of both the sick and the well in a community constitutes one of the most important features of any public health program directed toward the eradication of human tuberculosis The physician should insist on such chest x rays for all of his patients and the members of their families and especially with frequent repetitions of all who in any way or at any time have come in contact with one of his tuberculous patients

In addition to x ray examinations tuberculin tests in equally wide application should be urged If a chest x ray shows areas of calcification or fibrosis a tuberculin test is one of our best ways of determining their tuberculous etiology If the tuberculin test is positive it is probable that the lesion shown by x ray has a tuberculous etiology If the tuberculin test with increasing amounts of tuberculin remains negative then histoplasmin and/or coccidioidin should be used in further testing If one of these is positive this is an excellent confirmation of the absence of tuberculosis as has been suggested by the negative tuberculin test

The intradermal or intracutaneous route on the flexor surface of the forearm is preferable for a tuberculin test use the purified protein derivative [PPD] commencing with an initial dose of 0 0001 mg in healthy individuals over 16 years of age or 0 0000 mg for those in whom tuberculosis is more likely to be found If this dose does not give a positive reaction a second dose of 0 005 mg is to be employed For children in the better economic groups an initial dose of 0 000 mg may be used The test is read at 48 and 72 hours after injection A positive reaction consists of a papule of edema 5 mm in diameter with a surrounding zone of erythema It usually reaches its height in 48 hours Care must be taken to avoid tests especially tests with larger doses in patients with ocular skin and lymph node tuberculosis The Vollmer patch test is popular with pediatricians since the use of a needle is avoided It is satisfactory and gives a reasonably high degree of accuracy

Many state departments of health still employ old tuberculin. If this is to be used, the initial dose should be 0.1 cc. of a 1:10,000 dilution intracutaneously on the flexor surface of the forearm containing 0.01 cmm. of old tuberculin. If the initial test is negative, a dose of 0.1 cmm. is to be given, followed by a dose of 1.0 cmm., and if this dose is negative, by a dose of 5 cmm. and then 10 cmm. Since old tuberculin can and does produce false positive tests, it is being replaced more and more by the purified protein derivative.

It is particularly important that small children, especially those in families with tuberculous members, should be guarded against tuberculosis; every effort should be made to keep them healthy with good hygiene and adequate diet. By frequent x-ray examinations and tuberculin tests any tuberculosis developing in the children may be detected in its earliest stages and its treatment begun as soon as possible. The immunization of infants with *Bacillus Calmette Guerin* [B. C. G.] is being applied increasingly, with numerous reports of its safe effectiveness in reducing the incidence of tuberculosis in the young. More studies must be made, however, before it can be widely recommended. At this stage in this country it is more properly a tool for the public health authorities and belongs in their hands rather than in those of the individual physician. This also applies to the Vole vaccine, concerning which there are as yet insufficient data to warrant its use.

Milk, by spreading bovine tubercle bacilli, was formerly a major source of tuberculosis in man, especially of intestinal and lymph node tuberculosis. With widespread compulsory pasteurization of milk and tuberculin testing of cattle and with elimination from the herds of the positive reactors, this means of spreading tuberculosis to man has been greatly decreased and in many parts of the country almost completely eliminated. Every physician should insist that his patients and their families use only pasteurized milk.

Hansen's Disease: Leprosy

With our present knowledge the treatment of leprosy is in terms of a long range program. In the case of tuberculosis it is in terms of weeks and months; with leprosy it is a matter not of months but of years.

Of the benefits to be derived from good hygiene, cheerful surroundings, nutritious diet, adjusted hours of rest and outdoor exercises, physical therapy, and so on, there is no doubt, for carefully controlled

these things is a problem of both public and individual health of groups and of individuals of public agencies and of individual physicians the latter co operating with the former In all of this the recognition of the presence of tuberculosis in the individual as early as is possible is of the very greatest importance Without early diagnosis the tuberculous patient cannot be taught how to prevent himself from being a danger to others How this is to be done has been discussed already in the section on Isolation in Chapter I

The early diagnosis of pulmonary tuberculosis which is the form of the disease most responsible for its spread from man to man by x ray examination of the chests of both the sick and the well in a community constitutes one of the most important features of any public health program directed toward the eradication of human tuberculosis The physician should insist on such chest x rays for all of his patients and the members of their families and especially with frequent repetitions of all who in any way or at any time have come in contact with one of his tuberculous patients

In addition to x ray examinations tuberculin tests in equally wide application should be urged If a chest x ray shows areas of calcification or fibrosis a tuberculin test is one of our best ways of determining their tuberculous etiology If the tuberculin test is positive it is probable that the lesion shown by x ray has a tuberculous etiology If the tuberculin test with increasing amounts of tuberculin remains negative then histoplasmin and/or coccidioidin should be used in further testing If one of these is positive this is an excellent confirmation of the absence of tuberculosis as has been suggested by the negative tuberculin test

The intradermal or intracutaneous route on the flexor surface of the *forearm is preferable for a tuberculin test* use the purified protein derivative (PPD) commencing with an initial dose of 0 0001 mg in healthy individuals over 16 years of age or 0 00002 mg for those in whom tuberculosis is more likely to be found If this dose does not give a positive reaction a second dose of 0 005 mg is to be employed For children in the better economic groups an initial dose of 0 000 mg may be used The test is read at 48 and 72 hours after injection A positive reaction consists of a papule of edema 5 mm in diameter with a surrounding zone of erythema It usually reaches its height in 48 hours Care must be taken to avoid tests especially tests with larger doses in patients with ocular skin and lymph node tuberculosis The Vollmer patch test is popular with pediatricians since the use of a needle is avoided It is satisfactory and gives a reasonably high degree of accuracy

continuously over long periods — 6, 8 or 9 years If one seems toxic or unsatisfactory as it may another should be substituted Sometimes rest periods with no sulfone have seemed desirable With all of these drugs usually in the early stages of their use, severe erythema nodosum reactions with fever sometimes develop and require special management for this give 0 05 gm of antimony and potassium tartrate in 1 per cent solution or 0 315 gm of stibophen (Fuadin) in 6 3 per cent solution intramuscularly once a day for 3 days However, such reactions are a good prognostic sign for future improvement in the lesions of leprosy

In the ulcerative diffuse lepromatous (lazarine leprosy) and tuber culoid types ordinary doses of a sulfone may, and often do, aggravate the process For such patients smaller not larger doses of the sulfone are indicated The same applies with repeated episodes of distressing and painful neuritis With these antimony and potassium tartrate or stibophen, as described in the previous paragraph should be used Often injection of a 6 per cent solution of procaine hydrochloride around the infected nerve is indicated Cortisone has seemed helpful to some patients with leprous neuritis

The sulfones just discussed do have a very striking effect on the lesions of the disease clearing many of them An objection is that the drugs act slowly with significant clinical improvement not often seen for at least 6 months The type of improvement seems to be much the same for all the sulfones but it is hoped that additional drugs of this type will increasingly speed up the cure of the leprous lesions Recently, Faget has estimated that after 6 months of use of a sulfone, about 25 per cent of the patients will show improvement After 1 year this per centage increases to about 60 per cent after 2 years to 75 per cent, and after 3 years to almost 100 per cent

Clinical improvement is manifested in various ways Small nodules absorb completely Larger nodules disintegrate and leave a scar Ulcer ations heal in with granulation and cicatrix formation Mucous mem brane lesions heal nasal obstruction and epistaxes are relieved and the laryngitis improves frequently Not all skin and mucous membrane lesions however have been healed by drugs tried so far Sulfone therapy appears capable of checking the progress of conjunctival corneal and iridocyclitic leprous infiltration but is often not curative when the lesions have become marked Nerve lesions clear more slowly than many of the lesions of skin and mucous membranes

The most unsatisfactory features in the use of these drugs are the very long time 4 to 6 years or even longer often required to clear the

observations have shown that improvement in the disease always occurs with these measures alone Hence the importance of carrying out the general measures of treatment outlined in Chapter 1 is apparent

Chaulmoogra oil or one of its esters for many years the standard of treatment for leprosy has now been supplanted by the sulfones and related compounds with increasing use of one or the other of the antibiotics

Of the sulphones glucosulfone sodium (Promin), sulfoxone sodium (Diasone) and thiazolesulfone (Promizole) have had a longer and more extensive use than the others Sulfetrone promacetin and HES are drugs of this group which have been in use a shorter period of time but possibly will prove more effective than those in earlier use

Glucosulfone sodium (Promin) must be given intravenously with a dose of 1 0 gm gradually increased to 5 0 gm with a rest period every 2 weeks this makes it undesirable for the very long needed period of use Also it is mildly hemolytic

Thiazolesulfone (Promizole) is given by mouth as tablets or capsules 0 5 gm each giving at first 0 5 to 1 0 gm a day and then gradually increasing to 6 0 to 8 0 gm a day This proved more toxic than desirable and difficulties in manufacture rendered it costly

Sulfoxone (Diasone) sodium can be used effectively by mouth with an initial daily dose of 0 3 gm increased gradually to 0 6 to 0 9 gm a day and continued for 6 months with rest periods of 2 weeks every 2 months Following a rest period the course should be repeated for another 6 months

Sulfetrone has seemed in some ways preferable to the preceding agents but needs a longer period of years in use than has so far been possible Promacetin and HES (4 amino 4 beta hydroxyethylaminodiphenylsulfone) have seemed satisfactory but again need more years of use before their comparative value can be determined

Lowe has revived interest in diaminodiphenylsulfone which in his hands shows much promise Because of its cheapness and apparent excellent action it may become one of the more valuable agents in treatment The dose must be slowly increased from 100 mg daily for the first weeks to 00 mg daily for the next 2 weeks and then 300 mg daily

Another drug more recently under trial is amithiozone (tibione or 4-acetyl aminobenzaldehyde thiosemicarbazone) it seems a promising drug for further trial

It has been found that some one of these drugs can be given almost

a day increasing to 10 drops 3 times a day If long continued, alternate weeks of treatment and rest should be instituted

Prophylaxis

Gradually a saner attitude toward this disease is being taken the world over Although the disease is very mildly infectious, probably by the respiratory route a great fear of it has been handed down through religious literature Ordinary personal cleanliness and hygiene are usually sufficient to prevent acquiring leprosy, even when there is direct contact with persons afflicted Particular caution should be taken with children with periodic examinations being given so that treatment may be begun very early if infection is discovered

A new problem in prophylaxis has arisen because of the persistence of bacilli after treatment has brought about apparent healing of lesions Such patients must be regarded as still infective though since bacilli are usually much fewer their possible infectivity is not of great import

Recent evidence indicates the common cockroach as a carrier of the disease Hansen s bacillus has been found in cockroaches in contact with leprous patients Certainly flies mosquitoes cockroaches and other insects should be kept under control around leprous patients Chlorophenothane sprays and protection by screening and careful sanitation should help in the prevention of the disease

BIBLIOGRAPHY

Tuberculosis

1 Council on Pharmacy and Chemistry Chemotherapy of Tuberculosis in Man *Jour Amer Med Assoc* 1951 CXLVII p 53

2 Editorial Cortisone in Tuberculosis *Jour Amer Med Assoc*, 1951 CXLV p 907

3 Editorial Progress in Chemotherapy of Tuberculosis *N E J Med*, 1951 CCXLIV p 451

4 LURIE M B ZAPPASODI P DANNENBERG A M Jr and SWARTZ I B Constitutional Factors in Resistance to Infection the Effect of Cortisone on the Pathogenesis of Tuberculosi *Science*, 1951 CXIII p 234

5 Report of the Council on Pharmacy and Chemistry Current Status of Chemotherapy of Tuberculosis in Man *Jour Amer Med Assoc*, 1950 CXLII p 650

lesions of Hansen's bacilli and the fact that even after more years of continued use bacilli may still be present although decreased in number — in some patients they are present after all the years of treatment possible up to now

Consequently more research is needed in the hope of finding drugs that will be more rapidly effective in clearing lesions and in finally eliminating the infecting bacilli really specific drugs are needed to accomplish the latter Unfortunately with present drugs relapses do occur after the patient has stopped taking them

Certain of the antibiotics have been found to be effective or at least helpful in clearing leprous lesions if given daily over as long a time as possible before undesirable reactions develop This applies to streptomycin in an intramuscular dose of 1 0 gm daily or every 3 days and to aureomycin in a daily mouth dose of 1 0 to 1 5 gm Much more time is needed to evaluate these and possibly other antibiotics and to determine whether they should be used alone or with a sulfone or other drug

When the use of one sulfone gives undesirable reactions shifting to another sulfone is then indicated often this one will be free of such reactions If not an antibiotic should be substituted

Operative procedures are often required for correction of complications and sequelae For gangrene and bone necrosis excision is indicated Tracheotomy may be life saving in leprous laryngitis but the operation does not effect the course of the disease Healing of perforated ulcers of the foot is promoted by excision and curetting

The anemia of leprosy usually responds to the use of concentrated liver extract 1 0 cc thrice weekly and ferrous gluconate or sulfate 0 3 gm 3 times a day

Pain in the nerves involved with Hansen's bacilli may be most intractable In mild cases large doses of thiamine hydrochloride 50 to 100 mg given intramuscularly twice a day may be effective In more severe cases calcium gluconate 1 0 gm given intravenously daily for a week has a good sedative effect For the severe stubborn case the injection of a few drops of formic acid along the course of the nerve will relieve pain temporarily and 2 or 3 injections may give permanent relief

For an acute erysipiloid reaction of the skin sulfadiazine 4 0 gm initially followed by 1 0 gm every 4 hours penicillin 30 000 units every 4 hours or procaine penicillin 300 000 to 600 000 units intramuscularly daily is beneficial if given early For leprous erythema nodosum potassium arsenite (Fowler's Solution) is best begun with 3 drops 3 times

6 Symposium on Tuberculosis various authors *Am J Med* 1950 ix p 571
7 MITCHELL R S Ultimate Results from Pneumothorax *Am Rev of Tuberc* 1950 64 p 1 1 7
8 HINSHAW H C Therapy of Tuberculosis *Ann of Int Med* 1952 37 p 36

Hansen s Disease Leprosy

1 FACIT G H and ERICKSON P T Chemotherapy of Leprosy *Jour Amer Med Assoc* 1948 cxxxvi p 451
LOWE J Treatment of Leprosy with Diaminodiphenylsulfone by Mouth *Lancet* 1950 i p 145
3 SLOAN R N CHUNG HOON E K GODFREY HORAN M E and HEDGECOCK G H Sulfone Therapy in Leprosy Three Years Study *Hawaii Med J* 1950 ix p 301

biotics it is best, when possible to carry out in vitro tests of the isolated organism with these different antibacterials and then to use in treatment the ones of demonstrated effectiveness While this is being done, it is advisable to begin treatment with penicillin and if this is not clinically effective, to shift to the antibiotic that has been most effective in the in vitro testing

Penicillin should be given intramuscularly, in a dose of 50 000 units of the aqueous solution every 4 hours or in a dose of 300 000 to 600,000 units of procaine penicillin in aqueous suspension once a day in mild cases, twice a day in more severe cases or in widespread lesions Streptomycin when used should be given in a daily intramuscular dose of 1 gm

For those not responding well to the therapy just advised, a combination of penicillin streptomycin and sulfadiazine should be tried as follows Combined with penicillin and/or streptomycin, sulfadiazine or sulfamerazine should be given by mouth in an initial dose of 4 0 gm followed by 1 0 gm every 4 hours If the initial response is good, the penicillin or streptomycin may be discontinued after 3 weeks or 1 month but the sulfonamide should be continued for months if necessary, until all lesions have disappeared entirely and a soft scar remains When secondary invading organisms are present, which is frequent when a sinus tract has formed the therapy above will usually be adequate for them If the lesions do not respond to this therapy full doses of aureomycin or terramycin should be tried

The iodides so long an integral part in the treatment of chronic granulomatous processes — hastening by action as yet not understood the resorption of inflammatory tissue — still remain an important part in the treatment of actinomycosis The iodides are given in addition to the antibiotics especially when clearing up of the lesions is slow Tincture of iodine may be applied locally to tongue, mucous membrane and skin lesions Potassium iodide in increasing doses by mouth is often helpful and usually well tolerated A saturated solution should be used beginning with 0 3 cc 3 times a day and increasing each dose 0 1 cc up to a total of 3 to 5 cc 3 times a day If symptoms of iodism appear the drug should be stopped a rest period of 1 week given then the drug resumed, beginning again with 0 3 cc 3 times a day With symptoms of iodism another alternative may be tried that was found useful years ago by syphilologists After a rest period of a week resume the potassium iodide with large doses of 4 cc 3 times a day frequently iodism will not recur

With the pulmonary form of actinomycosis inhalation of a spray of ethyl iodide should be tried beginning with 0 25 cc, 3 times a day, and

PART III

FUNGOUS INFECTIOUS DISEASES

CHAPTER X

THE MYCOSES

Actinomycosis

In the treatment of actinomycosis in which the lesions are usually chronic infectious granulomata it is well to keep in mind that the disease wherever its location tends to become a chronic one and the treatment usually needs to be very prolonged Similar to tuberculosis long continued bed rest a nutritious high calorie diet and adequate fluids are essentials to promote the general health of the individual with actinomycosis

The more specific measures of therapy are much the same regardless of the location of the lesions The response to treatment and hence the prognosis vary considerably however depending largely on location The prognosis is best with lesions about the head and neck spoken of as the cervicofacial form This is also the form most frequent in occurrence Cases that have responded the least satisfactorily and so have the poorest prognosis are usually of the pulmonary variety the abdominal form has only a slightly better prognosis

The need for long duration and care in details of treatment must be emphasized whatever treatment is used Aureomycin penicillin sulfadiazine and streptomycin have proved beneficial At present penicillin and sulfadiazine and possibly aureomycin give the best results in treating patients with various clinical types of actinomycotic lesions Streptomycin has some value in treating patients with central nervous system involvement

Since a variety of species of the genus *Actinomyces* are causative agents for this disease and different strains vary in susceptibility to anti

biotics it is best, when possible, to carry out in vitro tests of the isolated organism with these different antibacterials and then to use in treatment the ones of demonstrated effectiveness While this is being done, it is advisable to begin treatment with penicillin and if this is not clinically effective to shift to the antibiotic that has been most effective in the in vitro testing

Penicillin should be given intramuscularly, in a dose of 50 000 units of the aqueous solution every 4 hours or in a dose of 300,000 to 600 000 units of procaine penicillin in aqueous suspension once a day in mild cases twice a day in more severe cases or in widespread lesions Streptomycin when used should be given in a daily intramuscular dose of 1 gm

For those not responding well to the therapy just advised a combination of penicillin streptomycin and sulfadiazine should be tried as follows Combined with penicillin and/or streptomycin sulfadiazine or sulfamerazine should be given by mouth in an initial dose of 4.0 gm followed by 1.0 gm every 4 hours If the initial response is good, the penicillin or streptomycin may be discontinued after 3 weeks or 1 month but the sulfonamide should be continued for months, if necessary until all lesions have disappeared entirely and a soft scar remains When secondary invading organisms are present, which is frequent when a sinus tract has formed the therapy above will usually be adequate for them If the lesions do not respond to this therapy full doses of aureomycin or terramycin should be tried

The iodides so long an integral part in the treatment of chronic granulomatous processes — hastening by action as yet not understood the resorption of inflammatory tissue — still remain an important part in the treatment of actinomycosis The iodides are given in addition to the antibiotics especially when clearing up of the lesions is slow Tincture of iodine may be applied locally to tongue mucous membrane, and skin lesions Potassium iodide in increasing doses by mouth is often helpful and usually well tolerated A saturated solution should be used beginning with 0.3 cc 3 times a day and increasing each dose 0.1 cc up to a total of 3 to 5 cc 3 times a day If symptoms of iodism appear, the drug should be stopped a rest period of 1 week given then the drug resumed beginning again with 0.3 cc 3 times a day With symptoms of iodism another alternative may be tried that was found useful years ago by syphilologists After a rest period of a week resume the potassium iodide with large doses of 4 cc 3 times a day frequently iodism will not recur

With the pulmonary form of actinomycosis inhalation of a spray of ethyl iodide should be tried beginning with 0 -5 cc 3 times a day, and

increasing in increments of 0.5 cc every 3 or 4 days until 1.0 to 3.0 cc are being given daily.

Until recently the surgical excision of local lesions even in the lungs was emphasized by many in the treatment of actinomycosis. Since the advent of the newer chemotherapeutic treatment opinion on this point has become divided for with the combined use of penicillin or streptomycin, sulfadiazine and the iodides surgery is often not necessary. On the other hand necrotic tissue should be removed. Sinus tracts may need to be excised. Careful judgment should be exercised and surgical excision employed when it may help in promoting the healing of involved tissues. High voltage x-ray irradiation may be useful in the same way as an adjunct to the therapy above.

Again it is to be emphasized that treatment may need to be very prolonged, as much as 4 to 6 months, with meticulous care in the regulation of medications so that the patient will not become intolerant of the drugs used before healing has become complete.

Sporotrichosis

Usually the lesions of sporotrichosis are localized in the skin and the patient is not ill enough to be confined to bed. The more disseminated forms involving skeletal or visceral structures are often acutely febrile and the general treatment outlined in Chapter I should be carried out.

Probably some one of the antibacterials will prove effective when clinical reports on their use are available. It would seem advisable to try them as discussed under Actinomycosis.

However, iodine in its various forms now is the most effective form of treatment of sporotrichosis and its use is advisable. Ulcerated lesions of the skin should be painted with tincture of iodine. Nodular lesions, if absorption is slow under the systemic treatment to be outlined, and abscesses form, should be punctured and drained and 1 per cent iodine solution should be injected. Radical incision or curettement should be avoided for such treatment tends only to prolong the process.

For systemic treatment the oral administration of progressively larger doses of potassium iodide as recommended for actinomycosis is advised. Its use must be continued for a long time, at least a month after apparent recovery, or relapse is likely to occur. X-ray therapy has been used by some but it is now generally considered to be only an adjuvant therapy; its use does not appear to hasten recovery. Heat therapy produced by

typhoid vaccine given intravenously or by the fever cabinet, has shown promise

Blastomycosis

Treatment of this condition is unsatisfactory Many agents have been employed, but none is of outstanding value The iodides and x ray seem to exert the most beneficial effect Owing to the tendency of patients infected with *Blastomyces dermatitidis* to become sensitive to the organism and react unfavorably to any attempt at vaccine therapy, it is necessary to test for sensitivity and if the patient is sensitive, to desensitize before commencing therapy This may be done with a stock or an autogenous vaccine in much the same manner as described for desensitization under Hay Fever The initial dose should be one that does not give a positive skin test following doses should be increased carefully to avoid reactions Usually 10 to 15 doses at 48- to 72 hour intervals are sufficient As soon as the patient is desensitized or if he is not sensitive originally a saturated solution of potassium iodide is given beginning with 3 drops 3 times a day after meals and increasing each dose by 1 drop until tolerance is reached or the patient is getting 50 drops 3 times a day Skin lesions are helped by x-ray therapy of 75 to 100 roentgens at 7- to 10-day intervals Usually a total dose of 1500 roentgens is sufficient Occasionally intravenous arsphenamine makes the organism more sensitive to iodides and x ray therapy

On a basis that certain of the diamidines may exert a fungostatic effect on *Blastomyces dermatitidis* several patients with blastomycosis have been treated with some success with stilbamidine and propamidine Stilbamidine may be tried beginning with a dose of 0 05 gm in 100 cc 5 per cent glucose given slowly intravenously and if well tolerated increased to 0 1 and 0 15 gm daily for 10 to 14 days After a two-week rest period the course of treatment may be repeated if necessary This drug is very toxic and great care must be taken in its use Unfortunately several months following the use of stilbamidine paresthesia of the face and at times agonizing neuritic pain often occur A 0 1 per cent solution of propamidine in 5 per cent dextrose in distilled water may be applied to surface lesions or into fistulae et cetera daily or every other day

In the pulmonary form of the disease inhalation of ethyl iodide, as described for actinomycosis, may prove helpful Sodium iodide intra

venously in a dose of 4.0 gm daily may be helpful in the systemic form. Vaccine therapy combined with iodides may give good results. Rectal instillation of ether and oil, 4 oz. of ether in a similar amount of oil given daily for 10 days after a cleansing soapsuds enema, has been of value in some cases.

Excision should not be done. The sulfonamides and antibiotics so far tried have proved of little value. Patients with the cutaneous type usually recover, but the lesions are usually very resistant to treatment. Those with the systemic type have a bad prognosis. Usually 90 per cent of the latter die in from 3 to 5 years irrespective of treatment. Prevention is difficult but care should be taken to avoid contact with infected individuals, especially if open wounds exist. Chewing grass or improper care of cuts and wounds may be sources of infection.

Chromomycosis (Chromoblastomycosis)

This rare disease is best treated by the excision and electrocauterization of early lesions supplemented by x-ray therapy. Large doses of potassium iodide may be employed but are not very helpful. Sulfamerazine apparently inhibits *Phialophora verrucosa* and should be used in full dosage. Iontophoresis with copper sulphate may be of some value. Penicillin is of little value. Other antibiotics should be tested out in vitro and if effective should be used in treatment. Amputation is not recommended since the disease does not become generalized.

Coccidioidomycosis

The fungus infection coccidioidomycosis occurs chiefly in two forms in which the prognosis is totally different — acute primary coccidioidomycosis and progressive disseminated granulomatous coccidioidomycosis.

Acute primary coccidioidomycosis. In this form the chief manifestation is pulmonary infiltration, the prognosis is usually very good, and no treatment other than symptomatic needs to be given. The therapy for these patients should be bed rest, a nutritious diet, and the general measures outlined in Chapter I. Bed rest should be continued until complete recovery is evidenced by (a) the absence of positive physical findings, (b) a normal chest x-ray or at least roentgen evidence of regressing lung lesions, (c) a normal sedimentation rate, and (d) a low titer or a complete absence of precipitins and complement fixation in the patient's

blood Isolation of the patient from others is not necessary, as dissemination from human to human is very unlikely, but it is well that the floors and walls of the rooms and wards housing patients with coccidioidomycosis be washed periodically with an antiseptic solution to prevent growth of the fungus in cracks and crevices and to minimize dust formation It is a matter of good hygiene when the patient is acutely ill with the pulmonary infection to burn or treat chemically all sputum dressings and discharges from skin lesions and sinuses Pulmonary cavitation if it occurs requires no additional treatment, except possibly pneumothorax or thoracic surgery in the rare patient with extensive pulmonary hemorrhage Sulfadiazine penicillin and other antibiotics have not been effective in acute primary coccidioidomycosis but chemotherapy does reduce secondary infections and therefore is useful

Progressive disseminated granulomatous coccidioidomycosis This form is known as both secondary coccidioidomycosis and coccidioidal granuloma It is a chronic disseminated usually fatal disease manifested by cutaneous subcutaneous visceral and osseous lesions It is considered rare for this second form to occur as a progression from the acute primary form although it may be possible if the primary form is not treated adequately as just described Patients with this form of coccidioidomycosis have usually been unaffected by a wide variety of drugs and vaccines used in the past These include the sulfonamides antibiotics iodides thymol antimony and potassium tartrate x ray therapy, and various vaccine extracts of the fungus If iodides are used, the patient exhibiting sensitivity should be desensitized with a vaccine of the fungus before administration

Antibiotic therapy is useful in controlling bacterial secondary invaders of the lesions

Paracoccidioidomycosis South American Blastomycosis

If the individual with paracoccidioidomycosis is found to be sensitive to extracts of *Paracoccidiodes brasiliensis* or *P cerebreformis* whichever organism may be found to be causative in the given case he should be desensitized as outlined for Blastomycosis before the iodides are started Increasing doses of iodides are to be used as described for Blastomycosis There is also evidence that the sulfonamides particularly sulfadiazine in doses of 1 0 gm 4 times a day may give dramatic temporary improvement and as improvement continues, the use of the sulfonamide should

go on The antibiotics should be tested in vitro and if effective they may then be given a clinical trial The disease however continues to be highly fatal

Cryptococcosis Torulosis European Blastomycosis

Known also as European blastomycosis cryptococcosis is to be treated as outlined for Blastomycosis with the additional therapy of surgical excision and drainage of local lesions supplemented by local x ray irradiation Usual doses of sulfadiazine such as 4 0 gm initially followed by 1 0 gm every 4 hours have been found to be effective in some instances Antibiotics should be tested for in vitro effects against the organism from the patient If one is found to be effective it should be used in treatment Repeated lumbar punctures give symptomatic improvement in patients with the meningitic or meningo encephalitic form of disease Recovery has been reported from such treatment alone but this is highly unusual

Histoplasmosis

There is no known specific therapy up to the present time for histoplasmosis More and more evidence is accumulating however for the belief that many particularly children and young adults with medi astinal calcified lymph nodes and fibroid calcified pulmonary lesions who are tuberculin insensitive and histoplasmin sensitive have recovered from the fungus infection histoplasmosis Hence it is the present opinion that histoplasmosis is far from being inevitably fatal as had been be lieved but that spontaneous recovery occurs quite frequently When the disease is widespread however involving lymph nodes liver spleen and intestines as it does the mortality is extremely high

In the treatment of histoplasmosis in other than the quiescent calcified form all of the general measures outlined in Chapter I should be utilized There is some evidence that pentavalent antimony in the form of sti bamine glucoside (Neostam) as used in the treatment of kala azar and leishmaniasis may be effective It should be dissolved in freshly distilled water to make a 5 per cent solution and then given immediately intra venously The initial dose per 100 pounds of body weight should be 0 050 gm and this should be increased daily or on alternate days to 0 1 gm 0 15 gm 0 2 gm then continued with 0 gm doses to a total of

2 6 to 2 8 gm per 100 pounds of body weight Stibamine glucoside may be quite toxic producing fever, cough, nausea, vomiting, diarrhea, lymphadenitis, and headache To prevent such toxic effects smaller amounts may need to be given on succeeding injections, or the interval between injections may have to be lengthened

The various sulfonamides penicillin, streptomycin the iodides and copper have been found to be ineffectual Local lesions may respond to deep x ray therapy

Maduromycosis Madura Foot

Since this infection may be caused by any one of a large variety of species of fungi of the genus Actinomyces there is no individual specific therapy The sulfonamides particularly sulfadiazine, in rather large doses by mouth, 4 0 gm initially followed by 1 0 to 1 5 gm every 4 hours, has been found to be somewhat effective against the disease itself but particularly so against secondary pyogenic organisms that so frequently occur later in the infection Antibiotics should be tested in vitro against the infecting organism and the effective one used Proper surgical excision and drainage of nodules and sinus tracts may be necessary Eventually amputation of the foot since that is the most common site of involvement may have to be resorted to There is no tendency to spontaneous healing

Aspergillosis

General treatment as outlined for Tuberculosis and in Chapter I should be instituted because of the chronic highly fatal nature of aspergillosis The standard treatment is potassium iodide as outlined for Blastomycosis In addition the patient should be tested with an autogenous vaccine of *Aspergillus fumigatus*, and if he is found to be sensitive vaccine therapy should be instituted beginning with a dilution to which the patient demonstrates no sensitivity A dusting powder of thymol iodide or 2 per cent thymol in 70 to 95 per cent alcohol may be applied locally to superficial lesions

Moniliasis

This disease caused by *Candida albicans*, formerly found most generally in debilitated patients is now appearing in patients who have been

on antibiotic therapy long enough to alter the bacterial flora sufficiently to favor the growth and invasion of the fungus Treatment of moniliasis depends in large part on the area of involvement Every effort must be made to correct any disease process such as diabetes mellitus infections malnutrition avitaminosis and other pathological states If the patient is receiving antibiotic therapy it should be discontinued as promptly as possible A well balanced diet supplemented with vitamins especially of the B complex is recommended

For cutaneous lesions the part should be kept dry Soaks for 30 minutes twice a day with a 1 4000 solution of potassium permanganate followed by the application of 1 per cent methylrosaniline chloride [gentian violet] are useful The staining caused by these agents is however frequently a problem When staining is undesirable and in areas where wet dressings cannot be applied effectively powders and solutions containing sodium and zinc caprylate undecylenic acid and its zinc salt propionic acid and its sodium and calcium salts and mixtures of these agents are all valuable and should be used For dry irritated areas an ointment containing sodium and zinc caprylate (Ointment Naprylate) one containing sodium propionate propionic acid sodium caprylate and zinc caprylate (Ointment Sopronol Propionate Caprylate Compound) and an ointment containing zinc undecylenate and undecylenic acid (Desenex Ointment Zincundecate) are all useful and usually give good results in 10 days to 2 weeks In macerated areas powders or solution of these fatty acids should be used For this purpose Powder Naprylate Powder Sopronol Propionates Caprylates Compound Desenex Powder Zincundecate or Desenex Solution Undecylenic Acid 10 per cent and sodium caprylate solution 20 per cent applied topically are all helpful The solutions should be diluted to 1 or 2 per cent when they cause irritation of the mucous membranes as they are likely to do if the surface is much irritated

For paronychia and onychia soaks with or applications of a thin paste of sodium perborate are helpful as is the application of a 5 per cent ammoniated mercury ointment X ray therapy is also useful in controlling these lesions

For oral mucous membrane lesions painting with 1 10 000 solution of methylrosaniline chloride [gentian violet] dissolved in 10 per cent alcohol twice a day for 3 or 4 days is usually successful A dilution of 1 100 000 of the dye may be used as a gargle

For vaginal lesions a jelly mixture of sodium and calcium propionate and propionic acid in a water soluble base (Propion Gel) is usually

effective A dose of 6 cc of the jelly applied morning and night in the upper portion of the vagina is recommended At the same time a small amount of the jelly should be applied externally Douches should be avoided during treatment The jelly should not be applied after the seventh month of pregnancy

In cases with pulmonary involvement increasing oral doses of potassium iodide and inhalations of ethyl iodide, as outlined under Blastomycosis are to be employed As with blastomycosis, the patient should be skin tested with an autogenous vaccine and if found to be sensitive, should be desensitized before iodine therapy is begun For massive pulmonary involvement, sodium iodide, 1 0 to 2 0 gm daily, as a 10 per cent solution intravenously or methylrosaniline chloride [gentian violet], 5 mg per kilogram of body weight made up to a 0 5 per cent solution and given intravenously daily or on alternate days, may be helpful Care must be taken to avoid venous thrombosis, which commonly occurs following this medication

There is not yet sufficient experience with the antibiotics actidione and patulin to recommend their use although activity against some strains of *Candida albicans* has been demonstrated

Dermatomycoses

Superficial fungus infection of the skin hair and nails is common and presents a difficult problem in treatment and prevention The usual infections of this type are tinea capitis generally found in children and caused by *Microsporum lanosum* or *Microsporum audouini* tinea corporis and cruris commonly caused by microsporum trichophyton or epidermophyton and dermatophytosis of the feet Athlete s foot, also resulting from trichophyton or epidermophyton

Tinea Capitis Treatment is based on accurate determination of the causative agent Patients infected with *M lanosum* should have the hair closely cropped and the areas mapped out with the Wood s lamp, this should be repeated at 10 day to 2-week intervals Daily shampoos to remove all the dead hair and detritus are necessary An ointment containing one of the fatty acids effective against the fungus should then be applied For this purpose the caprylate ointment (Ointment Naprylate) propionate caprylate ointment (Ointment Sopronol Propionates Caprylates Compound) or zincundecate ointment (Desenex Ointment Zincundecate) is effective The ointment selected should be rubbed

on antibiotic therapy long enough to alter the bacterial flora sufficiently to favor the growth and invasion of the fungus Treatment of moniliasis depends in large part on the area of involvement Every effort must be made to correct any disease process such as diabetes mellitus infections malnutrition avitaminosis and other pathological states If the patient is receiving antibiotic therapy it should be discontinued as promptly as possible A well balanced diet supplemented with vitamins especially of the B complex is recommended

For cutaneous lesions the part should be kept dry Soaks for 30 minutes twice a day with a 1 4000 solution of potassium permanganate followed by the application of 1 per cent methylrosaniline chloride [gentian violet] are useful The staining caused by these agents is however frequently a problem When staining is undesirable and in areas where wet dressings cannot be applied effectively powders and solutions containing sodium and zinc caprylate undecylenic acid and its zinc salt propionic acid and its sodium and calcium salts and mixtures of these agents are all valuable and should be used For dry irritated areas an ointment containing sodium and zinc caprylate (Ointment Naprylate) one containing sodium propionate propionic acid sodium caprylate and zinc caprylate (Ointment Sopronol Propionate Caprylate Compound) and an ointment containing zinc undecylenate and undecylenic acid (Desenex Ointment Zincundecate) are all useful and usually give good results in 10 days to weeks In macerated areas powders or solution of these fatty acids should be used For this purpose Powder Naprylate Powder Sopronol Propionates Caprylates Compound Desenex Powder Zincundecate or Desenex Solution Undecylenic Acid 10 per cent and sodium caprylate solution o per cent applied topically are all helpful The solutions should be diluted to 1 or per cent when they cause irritation of the mucous membranes as they are likely to do if the surface is much irritated

For paronychia and onychia soaks with or applications of a thin paste of sodium perborate are helpful as is the application of a 5 per cent ammoniated mercury ointment X ray therapy is also useful in controlling these lesions

For oral mucous membrane lesions painting with 1 10 000 solution of methylrosaniline chloride [gentian violet] dissolved in 10 per cent alcohol twice a day for 3 or 4 days is usually successful A dilution of 1 100 000 of the dye may be used as a gargle

For vaginal lesions a jelly mixture of sodium and calcium propionate and propionic acid in a water soluble base (Propion Gel) is usually

Tinea versicolor is more resistant and needs vigorous treatment for several weeks The involved areas should be thoroughly scrubbed with soap and water each day, and an ointment containing the most suitable strength of sulfur and salicylic acid as prescribed below, should be applied

Precipitated sulfur	3 0 to 6 0 gm
Salicylic acid	1 0 to 3 0 gm
Petrolatum to make	30 0 gm

Dermotophytosis of the Feet Athlete's Foot

This widely spread disease is the source of much distress and may cause serious infections Treatment varies somewhat depending upon the type of involvement Patients with moderately severe infections exhibiting moist areas of macerated epidermis and severe itching usually respond well to daily soaks for not longer than 1 week, with potassium permanganate solution, 1 4000 or warm boric acid solution, followed by the application of a fatty acid ointment such as Ointment Supronol Propionate-Caprylate Compound or Desenex Ointment Zincundecate at night and thorough cleaning drying and dusting of areas with Powder Sopronol Propionate Caprylate Compound or Desenex Powder Zincundecate during the day, which may be continued until relief is obtained

For patients with hyperkeratosis in the chronic non-inflammatory stage of the disease the application of a keratolytic ointment, such as Whitfield's Ointment half strength for 1 week to 10 days followed by the application of the fatty acid preparations recommended above, gives good results

Whitfield's Ointment	(half strength)
Salicylic acid	1 gm
Benzoic acid	[illegible] gm
White petrolatum to make	30 gm

It is absolutely necessary to prevent the patient from reinfecting himself during treatment and afterwards All socks worn by the patient should be boiled for 10 minutes if made of cotton If woolen socks are worn they should be adequately dry cleaned in order to destroy fungi contaminating them The patient's shoes should be exposed to formalde-

into the entire scalp morning and night Mild tincture of iodine U S P painted on individual lesions is also helpful Irritation by the iodine should be avoided

Patients should be prevented from spreading the infection by wearing skullcaps, and any pet infected with the fungus should be removed from all possible contact

Complete cure takes considerable time usually several weeks to months and parents and children should be alerted to this at the outset The Wood s lamp should be used to follow up the treatment Individually infected hairs should be epilated manually and careful mapping of infected areas noted so that treatment can be concentrated toward their eradication

Infection with *M audouini* is a more serious affair since it is at times extremely resistant to treatment The same therapy recommended for *M lanosum* may be tried but not infrequently the response is so slow or so poor that it is necessary to resort to a more drastic approach Salicylanilide N F (Ansadol) is useful and may hasten healing in some cases The simpler measures failing x ray epilation is justified This should be done for co operative children under the direction of a skilled dermatologist and an experienced x ray specialist The usual therapy recommended above should be continued after the x ray epilation

Prevention consists of avoiding all possible contact with sources of infections such as patients with the disease and fur bearing pets contaminated with the fungus Patients with the disease should wear protective skullcaps to prevent dessemination of the fungus Other individuals especially children in the household should be examined by the Wood s lamp since they may have slight degrees of infection Patients are usually cured when three successive examinations at 2 week intervals with the Wood s lamp shows no flourescence

Tinea Cruris, Tinea Corporis, Tinea Versicolor These fungus infections respond readily to treatment with the usual fungicidal agents For non macerated areas ointments containing caprylates propionic acid undecylenic acid or ammoniated mercury are all satisfactory Ointment Naprylate Desenex Ointment Zincundecate and Ointment Sopronal are excellent fatty acid fungicidal preparations Ammoniated mercury ointment 5 per cent U S P is also usually effective

For macerated areas or for places where ointments may promote maceration a powder or solution of one of the fungicidal fatty acids is recommended For this purpose Powder Naprylate Desenex Powder Zincundecate or Solution Sodium Caprylate is useful

8 RATCLIFFE H E and COOK W R Cryptococcosis Review of Literature and Report of Case with Initial Pulmonary Findings, *U S Armed Forces Med J* 1950 I, p 957
9 SCHOENBACH E B MILLER J M, GINSBURG M and LONG P H Systemic Blastomycosis Treated with Stilbamidine' *Jour Amer Med Assoc*, 1951 CXLVI, p 1317
10 THOMAS C C PIERCE H E and LABINER G W 'Sporotrichosis Responding to Fever Therapy *Jour Amer Med Assoc*, 1951 CXLVII p 1342

hyde vapor This can be done by sealing them for at least 48 hours in a can or box in which has been placed a wide mouth bottle containing a few cc of formaldehyde solution U S P Care must be exercised to prevent the formaldehyde solution from coming into contact with the leather

Prevention The feet must be kept dry at all times by thorough cleaning each day and the application of the fatty acid powders After bathing care must be taken to dry thoroughly between the toes If there is excessive perspiration of the feet soaking them for a few minutes in a 10 per cent formaldehyde solution 2 or 3 times a week for 2 weeks is helpful This treatment should not be carried out if there is active infection of the feet The formaldehyde solution should cover only the lower aspect of the feet as irritation of the thinner more sensitive skin of the dorsum of the foot is to be avoided

Bathroom floors should be scrubbed with 2 per cent cresol solution and bath mats soaked in it before laundering Infected persons should wear disposable paper slippers or walk on newspapers when barefoot to avoid contaminating the bathroom

BIBLIOGRAPHY

The Mycoses

1 FRAZIER C N and LEEPER R W The Treatment of Common Skin Diseases *Med Clin No Amer* September 1950 p 1480

JENKINS V E and POSTLEWAITE J C Coccidioidal Meningitis Report of Four Cases with Necropsy Findings in Three Cases *Ann Int Med* 1951 xxxv p 1068

3 LONG P H Clinical Use of Antibiotics *Med Clin No Amer* March 1950 p 307

4 MARTIN D S and SMITH D T Blastomycosis 1 A Review of the Literature 2 A Report of Thirteen New Cases *Am Rev Tuberc* 1939 xxxix pp 75 488

5 McVAY L V Jr GUTHRIE F and SPRUNT D H Aureomycin in Treatment of Actinomycosis *N E J Med* 1951 ccxlv p 91

6 MELENY H E Histoplasmosis (Reticulo Endothelial Cytomycosis) Review with Mention of 13 Unpublished Cases *Am J Trop Med* 1940 xx p 603

7 MOORE M Practical Points in Diagnosis and Treatment of Actinomycosis and Sporotrichosis *Postgrad Med* 1947 1 81

8 RATCLIFF H E and COOK W R "Cryptococcosis Review of Literature and Report of Case with Initial Pulmonary Findings *U.S Armed Forces Med J* 1950 1, p 957
9 SCHOENBACH E B MILLER J M, GINSBURG M and LONG P H Systemic Blastomycosis Treated with Stilbamidine' *Jour Amer Med Assoc*, 1951 CXLVI p, 1317
10 THOMAS C C PIERCE H E and LABINER G W Sporotrichosis Responding to Fever Therapy, *Jour Amer Med Assoc*, 1951 CXLVII p 1342

PART IV

VIRAL INFECTIOUS DISEASES

CHAPTER XI

VIRAL INFECTIOUS DISEASES OF RESPIRATORY TRACT

Common Cold Acute Coryza

Treatment There is no specific therapy for the common cold There is no sure preventive for it The methods of treatment available merely decrease the discomfort of a cold by relief of its symptoms and possibly shorten its duration by decreasing the number of complications and ameliorating their effects Sulfonamides and antibiotics have been ineffective against the cold but they do prevent bacterial complications Such negative and clinically unsatisfactory statements summarize our knowledge about the treatment of the common cold at the present time

Theoretically, the patient with a common cold should go to bed to reduce complications and prevent giving the cold to others Practically most patients with a cold unless very uncomfortable refuse to go to bed If they can be persuaded to stay at home and some can notably children by parental or school persuasion and compulsion this is certainly a worth while part of proper treatment Home stay during bad weather is highly desirable If there is fever with temperature above 100 F bed rest should be strongly advised when temperature is above 101 F it should be insisted upon

Diet should be simple and nutritious with ample fluid content of water and fruit juices milk cocoa tea and coffee Many physicians give a mild cathartic such as milk of magnesia vigorous catharsis is undesirable and not advised

The patient with a cold should be kept warm, particularly his feet If feet get damp change to dry stockings or socks and shoes should be made The patient should be protected from drafts, particularly if he is damp from perspiration, as is so often the case

Acetylsalicylic acid, phenacetin and codeine in varying combinations are very useful in ameliorating the aches and malaise usual to the common cold Such a mixture is Empirin Compound with Codeine Phosphate tablets

codeine phosphate	16 0 mg
acetylsalicylic acid	0 23 gm
phenacetin	0 16 gm
caffeine citrate	32 0 mg

to be taken every 3 or 4 hours if these discomforts persist Also, tablets of Edrisal with Codeine, another useful proprietary of common analgesics with amphetamine (benzedrine) sulfate and codeine sulfate, give relief

codeine sulfate	16 0 mg
benzedrine sulfate	2 5 mg
acetylsalicylic acid	0 16 gm
phenacetin	0 16 gm

A tablet every 3 or 4 hours is usually effective

Another favorite combination is codeine phosphate and papaverine hydrochloride, 15 mg of each given on a schedule, according to weight of patient increasing from 1 after breakfast and 2 at bedtime to 1 after each meal and 3 or 4 at bedtime

Measures to promote vasodilatation and sweating, such as hot foot baths and warm drinks — including hot toddies rum punches et cetera at bedtime — also often add to the patient s comfort Some physicians give opium and ipecac in the form of Dover s Powders 0 6 gm at night but this may upset the stomach

Hyperemia of mucous membranes especially the nasal ones should be diminished by instilling ¼ of a standard dropperful of an aqueous solution of 0 25 per cent phenylephrine (Neosynephrine) hydrochloride into the nose while the patient is reclining on his back with his head hyperextended over the side of the bed or couch to avoid overflow of the drug into the nasopharynx The drug is retained in the upper nasal passage in this manner for at least 2 minutes Much of the rebound hyperemia can be prevented by various antihistaminic agents such as tripelennamine (Pyribenzamine) hydrochloride 50 mg, given just before the vasoconstrictor is applied Some prefer to spray with a 1½

per cent solution of ephedrine hydrochloride if that is well tolerated but ephedrine is irritating to many in the concentration ordinarily used and tends to give considerable rebound hyperemia consequently nose and throat men are now limiting its use Amphetamine (Benzedrine) inhalation from some form of inhaler is convenient for the ambulatory patient Any of these vasoconstrictors should be used only in the acute phase of the cold and not oftener than every 4 hours since there is secondary hyperemia and chronic mucosal irritation from excessive use

If there is laryngitis or tracheitis the patient should refrain from talking If coughing is marked inhalations from a pan of boiling water containing a teaspoonful of compound tincture of benzoin or of oil of pine is often soothing Codeine phosphate 15 mg or dihydrocodeinone (Hycodan) bitartrate 5 to 15 mg 3 or 4 times in 24 hours may be needed to control the cough Persisting cough should be treated as described under Bronchitis

Complications of the common cold such as tonsillitis sinusitis otitis media mastoiditis bronchitis and bronchopneumonia should receive early treatment with penicillin or other antibiotic accompanied or followed by therapeutic measures as described elsewhere under these various headings

Prophylaxis Avoidance of contacts in crowded ill ventilated places particularly in seasons of prevalence of colds is advisable Patients with colds should restrict as far as possible contacts with others and should sneeze and cough into gauze or at least not toward another without an intervening hand Isolation of cold victims is advisable but unfortunately it is practically impossible The use of propylene glycol vapor and ultraviolet radiation in rooms where individuals congregate is seemingly of value in reducing the incidence of colds but much further investigation and perfecting of methods are still needed before a definite statement of its value is justified

Prophylactic use of sprays and gargles of irrigations of numerous vaccines of excess of vitamins of sulfonamides and penicillin preparations of antihistaminics of attempts at antiviral immunization of so called hardening measures of sun and artificial sun baths have all proved too little effective when there were careful studies with well selected controls, to justify advising the use of any of them The cold seemingly remains an unavoidable hazard of modern life with an average incidence of about 2 colds per year in any or all climates irrespective of what the individual does in the effort to avoid them

INFLUENZA

As yet there is no satisfactory specific treatment for this virus disease The patient with influenza should have prompt and absolute bed rest until the temperature has been normal for 2 or 3 days Care must be exercised in permitting activity, for relapses are common The pulse rate serves as a helpful guide to the amount of activity permissible A simple palatable, nutritious diet of bland consistency is indicated Fluids as desired or in sufficient amount to maintain urinary output of at least 2000 cc a day are given Nothing is gained by forcing fluids If constipation becomes a problem an enema usually suffices In the presence of high fever, headache and muscle aches and pains a cooling sponge bath, ice packs to the head and acteylsalicylic acid 0 6 gm every 4 hours, or opium and ipecac as Dover s Powder prove helpful Occasionally, with severe pain associated with nausea a combination of acetylsalicylic acid with phenacetin and caffeine (Empirin Compound) is indicated, or if discomfort is severe, a more effective analgesic such as meperidine hydrochloride 50 to 100 mg, methadone, 5 to 10 mg, or morphine sulfate, 8 to 15 mg may be used

Aureomycin may give prompt amelioration in patients with influenza A, so aureomycin in an initial mouth dosage of 2 0 gm followed by 1 0 gm every 4 hours should be tried in patients with influenza, even if identification of the type of causative virus cannot be determined Since influenza is caused by several strains of virus, it may be that an antibiotic effective against one strain will not be effective against another Consequently, clinical trial of aureomycin in any case is advisable

As a *prophylactic measure* against the possible development of a pneumonic infection the more seriously ill patients those already debilitated and those who are for any reason more likely to develop a complicating pneumonia should receive penicillin or aureomycin A satisfactory prophylactic level can be maintained with an aqueous suspension of penicillin procaine 300 000 units intramuscularly every 12 to 24 hours Aureomycin should be given by mouth in a dose of 1 gm 3 times a day Sulfadiazine may be employed also as a prophylactic in the usual therapeutic dosage If pneumonia develops, treatment should follow the pattern indicated for that disease

The upper respiratory tract irritation is ameliorated considerably by steam inhalation The occasionally severe cough may be relieved by 4 cc (1 teaspoon) of the following mixture taken every 3 to 4 hours as needed

codeine phosphate	0 5 gm
ammonium chloride	10 0 gm
syrup of citric acid	60 0 cc
syrup of tolu, to make	120 0 cc

An intractable cough is usually benefited by dihydrocodeinone (Hycodan) bitartrate 5 to 15 mg 2 or 3 times a day or the syrup of Hycodan used similarly Very effective also is a mixture of equal parts of syrup of Hycodan and a syrup of glyceryl guaiacolate plus desoxyl-phedrine hydrochloride (Robitussin), 1 teaspoonful 3 or 4 times in 24 hours

If circulatory collapse appears it should be treated as described for Pneumonia

During convalescence care must be taken to avoid a too rapid return to normal activities Rest both mental and physical, in adequate amounts is essential if the commonly experienced mental and physical depression is to be avoided or kept to a minimum Pleasant surroundings nutritious diet, fresh air, and reassurance are all very helpful for satisfactory con valescence

Prophylaxis Transmission is accomplished mainly by the air borne route and may be markedly reduced by the use of ultraviolet irradiation and propylene glycol vapor in such public gathering places as schools churches theaters and places of business Vaccination with multiple-type vaccine made from the causative virus has proved reasonably ef fective and will prevent infection in a good percentage of exposed individuals Immunity persists for at least 1 year A dose of 1 0 cc subcutaneously or 0 1 cc intracutaneously for adults or of 0 5 cc sub cutaneously repeated in 1 week for children under 12 years of age is recommended Approximately 2 per cent of those vaccinated develop febrile reactions localized redness swelling and tenderness quite similar to the reactions of certain individuals sensitive to typhoid vaccine The reaction usually lasts about 1 day Individuals allergic to egg protein should not receive the vaccine or should receive it in small doses under careful observation to prevent anaphylactic reactions Since the re actions may be severe and as many as 50 per cent of those vaccinated may develop some disturbance following the vaccination it is not wise to vaccinate indiscriminately Weak, highly susceptible or aged patients should be protected by vaccine

Prevention during Epidemics When influenza appears in rapidly spreading form various efforts have been made to slow its spread such

as advising individuals not to congregate in numbers, to keep out of street cars and to stay at home as much as possible Schools usually, theaters sometimes, churches rarely have been ordered closed The wearing of masks has been advised, and in some cities this has been done very extensively These measures may do good but there is no convincing evidence Possibly some of these measures increase panic and do harm The most effective measure, if it could be enforced, would be to make every individual stay at home when the very first symptom occurs and go to bed as soon as fever appears The latter undoubtedly would work to decrease the severity of the influenza and lessen incidence of complications

Infectivity in influenza seems to take place during the period of incubation and to lessen greatly or even disappear as soon as symptoms become prominent Apparently there is a person to-person contact infectivity It seems wise for all in contact with those having influenza to practice the usual measures against close person to person contacts to avoid coughed out respiratory droplets to protect the hair, to wear gauze masks and to use sterilizable gowns Dishes, bed linen sputum and used gauze should be sterilized by boiling or heat process as soon as possible

Non-Bacterial (Viral) Pneumonia

The treatment of this form of pneumonia can be discussed under two headings (1) antibiotic therapy and (2) symptomatic and general measures

The most effective antibiotic up to the present time has been aureomycin with reports of excellent results from its use on patients Some cases of non bacterial pneumonia have been shown to be caused by varieties of rickettsiae and these also have had excellent results from the use of aureomycin Many cases of non bacterial pneumonia have been treated in the past with sulfonamides especially sulfadiazine, with penicillin and with streptomycin but the results have been very largely negative Consequently aureomycin seems the antibiotic of choice for these patients and should be given in a dose of 1 0 gm every 4 to 6 hours in acute illness and continued at a dose of 2 to 3 gm a day for at least 3 days after the fever has returned to normal Terramycin may be tried

Sulfonamides, penicillin, and streptomycin have now been shown to

be ineffective in non bacterial pneumonia and should not be used unless a secondary infection sensitive to one of them develops

General measures and symptomatic therapy are of decreasing importance in relation to the promptness and effectiveness of antibiotic therapy Those measures discussed under General Measures for the Treatment of Bacterial Pneumonias are to be applied in the treatment of viral pneumonia Adequate bed rest continued well into convalescence has been found to decrease significantly the incidence of relapse An adequate nourishing diet, the proper administration of liquids for fluid balance and oxygen for cyanosis are indicated as with other types of pneumonia The use of tincture of benzoin in steam inhalations may be very soothing or plain steam by increasing the humidity of the room will help to comfort a tracheitis and distressing cough Acetylsalicylic acid 0 6 gm every 4 to 6 hours may be used as an antipyretic although some patients with viral pneumonia are thereby made uncomfortable with excessive sweating Codeine phosphate 15 to 30 mg or dihydrocodeinone (Hycodan) bitartrate 5 to 15 mg should be given 3 or 4 times in 24 hours as needed to control the severe cough which is often very discomforting and exhausting

Some advise repeated small transfusions of whole blood particularly when an anemia exists

The signs of viral pneumonia visible by x ray may continue to be present as long as several weeks after the patient feels well and is without fever or other manifestations of the disease Usually in this stage no treatment is necessary it is well however to continue measures appropriate to convalescence until all the signs of the disease have disappeared

BIBLIOGRAPHY

Viral Infectious Diseases of the Respiratory Tract

1 COLLINS H S WELLS E B GOCKE T M and FINLAND M Treatment of Primary Atypical Pneumonia with Aureomycin *Am J Med* 1950 viii p 4
2 FINLAND M WELLS E B COLLINS H S and GOCKE T M Aureomycin in the Treatment of Influenza and Certain Other Acute Respiratory Infections with or without Pneumonia *Am J Med* 1950 viii p 21

CHAPTER XII

VIRAL COMMUNICABLE DISEASES (EXANTHEMATA)

MEASLES

The treatment of an acute attack of measles is entirely symptomatic, with particular emphasis on the prevention of complications The patient should be placed in a warm, comfortable room isolated to prevent spread of the infection to others and, just as important, to avoid infection with streptococci and other organisms that cause complications Therefore, all persons who enter the sick room should practice strict isolation precautions by wearing masks and gowns A good wholesome diet should be instituted, but since the uncomplicated disease is of such short duration special care of nutrition need not usually be given Fluids should be employed liberally

Since photophobia is a prominent symptom, the patient should be shielded from bright light and the eyes bathed with boric acid solution Fever is seldom a troublesome symptom but, when high, may be combatted with small doses of acetylsalicylic acid 0 2 to 0 3 gm by mouth, or, better, by sponge baths or tepid baths gradually cooled For distressing cough dihydrocodeinone (Hycodan) bitartrate in oral doses of 5 to 15 mg 3 or 4 times in 24 hours for adults one fourth this dosage for children under two one half for children from two to adult age codeine sulfate in doses of 30 to 60 mg for adults and proportionately less for children according to weight or inhalations of steam containing tincture of benzoin are useful The cough should be suppressed but not prevented completely When desquamation of the skin begins the skin should be oiled daily after a warm bath The mouth and nostrils should be kept clean, but oiling of the mucous surfaces should be avoided Convalescence should not be hurried

The various sera discussed later for the prevention or the amelioration of measles are without appreciable effect after the rash has appeared The sulfonamides and penicillin are without effect on the course of the disease but are most useful in treating the pyogenic complications of pharyngitis tracheitis bronchitis pneumonitis, and otitis media There

be ineffective in non bacterial pneumonia and should not be used unless a secondary infection sensitive to one of them develops

General measures and symptomatic therapy are of decreasing importance in relation to the promptness and effectiveness of antibiotic therapy Those measures discussed under General Measures for the Treatment of Bacterial Pneumonias are to be applied in the treatment of viral pneumonia Adequate bed rest continued well into convalescence has been found to decrease significantly the incidence of relapse An adequate nourishing diet the proper administration of liquids for fluid balance and oxygen for cyanosis are indicated as with other types of pneumonia The use of tincture of benzoin in steam inhalations may be very soothing or plain steam by increasing the humidity of the room will help to comfort a tracheitis and distressing cough Acetylsalicylic acid 0 6 gm every 4 to 6 hours may be used as an anti pyretic although some patients with viral pneumonia are thereby made uncomfortable with excessive sweating Codeine phosphate 15 to 30 mg or dihydrocodeinone (Hycodan) bitartrate 5 to 15 mg should be given 3 or 4 times in 24 hours as needed to control the severe cough which is often very discomforting and exhausting

Some advise repeated small transfusions of whole blood particularly when an anemia exists

The signs of viral pneumonia visible by x ray may continue to be present as long as several weeks after the patient feels well and is without fever or other manifestations of the disease Usually in this stage no treatment is necessary, it is well however to continue measures appropriate to convalescence until all the signs of the disease have disappeared

BIBLIOGRAPHY

Viral Infectious Diseases of the Respiratory Tract

1 COLLINS H S WELLS E. B GOCKE, T M and FINLAND M Treatment of Primary Atypical Pneumonia with Aureomycin *Am J Med* 1950 viii p 4

2 FINLAND M WELLS E. B COLLINS H S and GOCKE, T M Aureomycin in the Treatment of Influenza and Certain Other Acute Respiratory Infections with or without Pneumonia *Am J Med*, 1950 viii p 21

complete protection After the sixth day amelioration of the attack will probably occur The use of convalescent human serum gives few toxic effects

Pooled normal adult serum is usually readily available, but its low potency necessitates the injection of large volumes, which is undesirable, particularly in small children It gives full protection when given before the fourth day after exposure in only about 55 per cent of cases, with attenuation in 25 per cent and failure in 20 per cent The dosage of this material ranges from 10 to 80 cc given subcutaneously or intra muscularly Toxic effects are few Normal pooled adult serum (adult immune serum) may be obtained concentrated in powdered form in the frozen state, which, when reconstituted with a small volume of water, is both safe and effective for the prophylaxis of measles It must be re membered that human serum especially pooled human serum may contain the virus of homologous serum infectious hepatitis, and the risks attendant to that disease must be assayed before human serum is employed

Placental immune globulin readily available and requiring only a small inoculum causes local and systemic reactions of varying severity in a considerable number of inoculated individuals It affords complete protection in approximately 65 per cent of individuals and attenuation in 30 per cent, with a failure rate of 5 per cent The dose should be 0 1 cc per pound of body weight for prevention 0 025 cc per pound for attenuation and a total dose of somewhere between 1 0 to 5 0 cc

Fraction II of gamma globulin is a newer product of gamma globulin, made available through the American Red Cross and is about as effective as the others and the least toxic of any of the antibody substances It is effective for protection in about 70 per cent of cases and for attenuation in 27 per cent with a 2 per cent failure rate A dose of 0 1 cc per pound of body weight within an interval of 5 days after exposure is recommended for protection and a dose of 0 025 cc per pound within the first 5 days for modification of the disease More definitive results may be obtained either for protection or attenuation by varying the dose rather than the interval between exposure and injection

Rubella German Measles

Treatment Usually a mild disease of brief duration rubella needs little in the way of treatment There is no known effective specific

is no specific treatment for measles encephalitis but certain of the man ifestations may be controlled by adequate sedation with phenobarbital 0 1 to 0 2 gm paraldehyde 4 to 12 cc or, preferably, chloral hydrate 0 6 to 1 0 gm, or for very severe convulsive states rectal tribromethanol (Avertin) in amylene hydrate anesthesia, 0 05 to 0 1 cc per kilogram of body weight

Prophylaxis The prevention or modification of measles by means of passive transfer of human antibodies is now well established Four sources of such antibodies have been developed for injection (1) con valescent measle serum (2) pooled normal adult serum (3) globulin derived from human placentas and (4) a serum gamma globulin concentrate derived from pooled normal human plasma known as fraction II The last is the most recent development and seems to be the most effective and also the least toxic

With the use of any of these substances whether the measles is prevented or merely modified in its course depends upon the amount of antibodies injected and the time interval after exposure before the injection is given Too small an amount of antibodies or an injection given after the ninth day following exposure will not usually alter the course of the disease

Under certain circumstances, such as the presence of another particularly debilitating disease or in an institutional epidemic or possibly in the very young it may be highly desirable to prevent measles altogether once exposure is known to have occurred This is accomplished by rather large doses of antibodies given in the first few days after exposure preferably the first 4 The disadvantage of such passive protection is the fact that it lasts only 2 or 3 weeks after which the child is again susceptible to measles and all its complications It is the present con census of opinion that usually and particularly in the pre school age child an attenuated form of the disease should be allowed to occur, which gives an active immunity persisting throughout life This is ac complished by giving a smaller dose of antibodies 5 to 7 days after exposure Such attenuated cases are also less likely to develop the secondary bacterial complications Usually no effect on the disease will be obtained after the tenth day following exposure regardless of the dosage employed

Convalescent human serum not so readily available gives full pro tection in 75 per cent of cases and causes attenuation in 17 per cent with a failure rate of 8 per cent A dose of 3 to 6 cc injected subcuta neously or intramuscularly within 4 days after exposure usually gives

should be adequate Regular daily bowel movements should be obtained

Symptomatic therapy during the acute stage of the illness is to be directed against fever, nausea, vomiting, and pain in the back Fever is usually of short duration and is controlled readily with antipyretics such as acetylsalicylic acid 0 3 to 0 6 gm every 3 or 4 hours Cool sponging or a tub bath is useful in soothing the skin lesions If there is delerium with high fever, cold packs may be necessary For severe toxemia with severe eruption, continuous warm baths may be advisable

Nausea, and particularly vomiting may become quite intractable It may be relieved by giving only cracked ice by mouth for a day or two Some have reported direct benefit for vomiting by intravenous infusions of 5 per cent glucose The vomiting ceases usually with the onset of the eruption Parenteral glucose and saline may be necessary for several days to combat dehydration The salicylates given for fever may control the back pain if not, a combination of analgesics or analgesics plus a sedative may need to be given as advised in Part 1 for pain during infection

Considerable care should be exercised in the treatment of the eruption but therapy should not be overdone The application of many types of ointments and solutions may only lead to more disfigurement A daily warm tub bath with soap and water, followed by painting the lesions with mild tincture of iodine U S P 2 per cent, or dusting them with talcum powder is useful If the pocks are painful particularly on the face hands or feet they may be softened with boric acid wet packs Secondary invading organisms may be controlled by penicillin or one of the wider spectrum antibiotics such as aureomycin given in usual doses systemically

When crusts begin to form they should be kept soft with oil glycerin or vaseline For the odor dilute phenol solution (2 per cent) is best During convalescence frequent bathing followed by the application of oil daily will soften the crusts and minimize scarring Convalescence is not to be considered established until the skin is free from all crusts—perfectly smooth and clean

Complications Conjunctivitis a common complication should receive careful attention with frequent cleansing of the eyes with boric acid solution and the applications of vaseline to the margins of the eye lids to prevent them from sticking together Ice cold compresses may add to the comfort If the corneae become involved the services of an ophthalmologist should be obtained promptly

The mouth and throat should be cleansed carefully several times a

therapy serum antibiotic or chemotherapeutic agent If symptoms are unpleasant they should receive symptomatic treatment as in other infectious diseases Bed rest during the few febrile days of rubella is desirable but is not obligatory The only serious aspect in the clinical course of rubella is the occasional encephalitis which infrequently appears in young adults and is similar to that occurring with measles If pregnant women contract rubella especially in the first trimester of pregnancy, there is a definite not inconsiderable probability that their babies will be born with a congenital lesion or abnormality most often congenital cataracts or a congenital heart lesion

Prophylaxis Isolation of the rubella patient for 3 days from the appearance of the rash has seemed sufficient to restrict spread of the disease Except for pregnant women prevention of rubella is usually regarded as undesirable If the child has rubella in later years the pregnant female will be spared from the probability of congenital lesions in her baby to have had rubella is an asset to the pregnant woman If she has not had rubella the pregnant woman should be guarded against contact with rubella patients and with those exposed to such for a period of 3 weeks following their exposure

There is no satisfactory effective prophylactic procedure although *there is some evidence that the intramuscular injection of gamma globulin* has some effective protective value Until something more effective is available it should be given to pregnant women who have not had rubella at the commencement of their pregnancy and to children who have not had rubella and are likely to come in contact with these pregnant women or who are ill or recovering from a serious illness

Smallpox and Vaccination

The treatment of smallpox consists primarily in the amelioration of symptoms by symptomatic therapy attention to the pustules and crusts of the rash and the prevention or treatment of bacterial complications

Complete segregation of the smallpox patient is of utmost importance Each attendant should be re vaccinated and must practice strictest precautions against infection with mask and gown All linens should be placed promptly in per cent phenol and then boiled All dressings and sputum should be burned

The diet should be largely liquid advancing to soft solids and regular diet as the patient s condition permits and improvement continues Fluids

should be adequate Regular daily bowel movements should be obtained

Symptomatic therapy during the acute stage of the illness is to be directed against fever, nausea, vomiting, and pain in the back Fever is usually of short duration and is controlled readily with antipyretics such as acetylsalicylic acid 0 3 to 0 6 gm every 3 or 4 hours Cool sponging or a tub bath is useful in soothing the skin lesions If there is delerium with high fever, cold packs may be necessary For severe toxemia with severe eruption, continuous warm baths may be advisable

Nausea and particularly vomiting, may become quite intractable It may be relieved by giving only cracked ice by mouth for a day or two Some have reported direct benefit for vomiting by intravenous infusions of 5 per cent glucose The vomiting ceases usually with the onset of the eruption Parenteral glucose and saline may be necessary for several days to combat dehydration The salicylates given for fever may control the back pain if not, a combination of analgesics or analgesics plus a sedative may need to be given as advised in Part 1 for pain during infection

Considerable care should be exercised in the treatment of the eruption but therapy should not be overdone The application of many types of ointments and solutions may only lead to more disfigurement A daily warm tub bath with soap and water, followed by painting the lesions with mild tincture of iodine U S P 2 per cent, or dusting them with talcum powder is useful If the pocks are painful particularly on the face hands or feet they may be softened with boric acid wet packs Secondary invading organisms may be controlled by penicillin or one of the wider spectrum antibiotics such as aureomycin, given in usual doses systemically

When crusts begin to form they should be kept soft with oil, glycerin or vaseline For the odor dilute phenol solution (2 per cent) is best During convalescence frequent bathing followed by the application of oil daily will soften the crusts and minimize scarring Convalescence is not to be considered established until the skin is free from all crusts — perfectly smooth and clean

Complications Conjunctivitis a common complication should receive careful attention with frequent cleansing of the eyes with boric acid solution and the applications of vaseline to the margins of the eye lids to prevent them from sticking together Ice-cold compresses may add to the comfort If the corneae become involved the services of an ophthalmologist should be obtained promptly

The mouth and throat should be cleansed carefully several times a

day, using the alkaline aromatic solution N F diluted one half for mouthwash Glycerine or oil should be applied to the nostrils to prevent the formation of crusts

Laryngitis from the presence of pocks may become a serious complication, and if edema ensues tracheotomy may need to be carried out

Bronchitis and bronchopneumonia due in part to the disease and in part to pneumonococci streptococci and staphlococci, are often combatted successfully, depending upon the susceptibility of the invading organism with sulfadiazine sulfamerazine penicillin or aureomycin in the usual adequate doses

Vaccination Proper vaccination and re vaccination are known to be the most important preventive measure

Vaccination within 4 days after exposure will almost always prevent the occurrence of the disease All persons exposed should be vaccinated or re vaccinated and isolated for 16 days Unless there has been direct exposure, it is thought best not to vaccinate women during menstruation or persons with open skin lesions of any kind Bone tuberculosis is considered by many a definite contraindication to vaccination

The technique of vaccination should be carried out as follows Either calf vaccine virus or chick embryo culture virus should be used The site upper arm in the male outer thigh in the female should be cleansed with acetone or ether and this allowed to dry A drop of virus is placed on the cleansed area and a needle point held parallel to the extremity, is pressed into the skin about 10 times care must be taken not to puncture the skin The remaining material is wiped away and the vaccination site kept uncovered by any form of bandage or protective shield When the pustule appears about the fifth or seventh day a light piece of gauze is taped over the area From this time no cleansing of the area should be carried out until a firm crust is established Lack of previous immunity is indicated by a large red areola with a central vesicle that becomes a pustule which in turn becomes covered by a crust in 8 to 14 days An areola with elevation of the skin but without pustule or crust in 3 to 7 days indicates partial immunity With immunity present there will be only redness itching and, perhaps slight skin elevation lasting 48 to 72 hours If none of the reactions above has occurred it may not necessarily mean adequate immunity but may signify failure of the vaccination to take If uncertain the procedure may be repeated at 2 week intervals for several attempts

Chick embryo culture virus may be given intradermally with this ulceration does not usually follow

The duration of immunity from vaccination is not known accurately but is thought to be about 5 years on an average, probably less in Negroes than in whites Children should be vaccinated at 6 months of age upon entering school and again at puberty Adults should be re vaccinated at the time of exposure or before entering an area in which smallpox is known to exist Physicians nurses, or others in direct con tact with an epidemic should be re vaccinated at once, regardless of the previous date of vaccination unless it is a matter of only several weeks

Chickenpox

The usual mild course of this virus infection calls for little therapeutic effort However the clinician should be constantly on guard against complications which may be most serious

There is a close relationship between the virus of this disease and herpes zoster The similarity of the skin lesions epidemiological and immunological data as well as the close similarity of the intranuclear inclusion bodies all tend to link these two diseases However there is no definitely proved relationship as yet Certainly cross immunity is not perfect

In the treatment of chickenpox bed rest, isolation, and measures to prevent secondary infection of the vesicles by scratching — such as clean linen and clothing well clipped finger nails thoroughly scrubbed with soap, water and alcohol and strict cleanliness of the skin are rec ommended Phenolated Calomine Lotion N F will allay some of the itching as will the antihistaminic drugs — diphenhydramine (Benadryl) and tripelennamine (Pyribenzamine) 10 to 50 mg 3 times a day for children and 25 to 100 mg 3 times a day for adults Bacitracin or aureomycin ointment is indicated for complicating local infections such as erysipelas impetigo furuncles and abscesses penicillin and aureo mycin given for their systemic effects are of distinct value if broncho pneumonia or skin ulceration appears

It is doubtful that convalescent serum is of value in preventing this disease It may be tried in a dose of 10 to 15 cc intramuscularly The serum should be secured within 1 month of an attack in order to obtain the best results Vaccination and gamma globulin are of questionable value

CHAPTER XIII

VIRAL DISEASES OF THE CENTRAL NERVOUS SYSTEM

Poliomyelitis

The management of poliomyelitis is divided into four parts (1) the acute stage (a) pre paralytic (b) abortive and (c) paralytic phases (2) the recovery stage (3) the convalescent stage and (4) the residual stage

The Acute Stage

Since statistical studies have shown that 60 per cent of poliomyelitis cases occur under the age of 10 years and over 80 per cent under the age of 15 years in any child or adolescent who during the hot summer and fall months of the year develops headache sore throat, or fever the possibility of poliomyelitis should be considered until proved other wise Only with such an attitude particularly when there is no epidemic can treatment be started early a factor so important in the ul timate outcome of the case A dictum may be presented that although many patients may so be diagnosed incorrectly with poliomyelitis it is better to be suspicious than always correct The earliest recognition with proper treatment has been shown to reduce significantly the immediate mortality rate, and many disabilities can be averted with early and per sistent routine care

The Pre paralytic Phase Except in epidemics as already emphasized, this phase may be most difficult to recognize and yet the most can be accomplished at this time This stage which may last from 3 to 5 days after the onset of the disease may be recognized by restlessness apprehension fever and a slightly stiff neck The latter is the first specific sign suggesting anterior poliomyelitis and is confirmed by lumbar puncture demonstrating at first leucocytosis and several days later pleocy tosis composed mainly of lymphocytes in the spinal fluid Another very early sign is the absence of abdominal reflexes

and gamma globulin are of no value and their use is not advised Blood plasma or whole blood may be given to restore plasma proteins or to correct an existing anemia

As the fever falls, toward the end of this stage of the disease muscle tenderness spasm, contraction and pain may appear For this, heat in any form is beneficial, including the hot pack treatment of Sister Kenny of Australia At present this treatment is one of the popular methods of applying heat to the muscles in this disease It is very effective in relaxing muscle spasm but it is not to be used to the exclusion of other forms of therapy for poliomyelitis The Kenny method is in no sense a cure for there remains after the use of her method the same percentage of partly paralyzed patients as before

With the use of the Sister Kenny treatment in this stage as well as in the paralytic stage to be described later three guides should be followed First the greatest care should be exercised in the amount of heat and the duration of application particularly if the patient s own temperature exceeds 103°F by mouth It is felt that general heating which results from packing might be sufficient to cause further rise in temperature that may be unfavorable to the patient At the same time the majority of cases of anterior poliomyelitis occur in children in whom there is often instability of the temperature regulatory mechanism Secondly to avoid prolonged dilatation of cutaneous and other peripheral capillary blood vessels with excessive passive congestion in muscles that are not being moved or exercised leading in turn to stiffness fibrosis and shortening heat should be applied intermittently and for not more than 1 or 2 hours at a time When hot packs are used either as a full pack or prone pack (see below) they are to be applied at intervals of from 15 minutes to 2 hours depending upon the acuteness of the condition The average is from 6 to 8 complete packs, carried out between 8 a m and 8 p m In severe cases packs may have to be applied around the clock As the handling incidental to packing may be quite exhausting it is desirable for the patient to get the necessary rest during the night Thirdly with the patient in a prone position during the treatment moist woolen packs should be applied over the spine and to each extremity in which there is muscle soreness change of muscle tone or beginning weakness To avoid handling as much as possible the packs should not be wrapped around but simply laid on the involved extremity or the spine This method of the application of heat is spoken of as *prone packing*

Woolen packs may be cut from old blankets immersed in boiling

As soon as it is decided that the patient has poliomyelitis, he should be protected from exertion, tiring procedures, and long ambulance trips, if possible treatment should be instituted immediately

It is most important to place the patient at complete bed rest with quiet, considerable care must be given to his position in bed A firm mattress preferably with bed boards between it and the springs will aid in giving proper support to the muscles of the back A foot board should be put into place, providing a smooth surface against which the feet may be braced in a position of 90 dorsiflexion and neutral with respect to rotation The board should be on blocks so that there is a 4-inch space between it and the mattress for the heel point

The patient should not be allowed to thrash about excessively and, if necessary, should be kept quiet with the use of mild sedatives such as phenobarbital, 15 to 30 mg according to the age and the restlessness manifested Salicylates such as acetylsalicylic acid 0 3 to 0 6 gm every 3 to 4 hours, are useful for severe headache or the ordinary muscular pain when it is causing discomfort In rare cases in which there is marked severe pain, methadone in doses suitable to the age of the patient may be given

A full nourishing diet with proper fluid balance must be maintained as outlined in Part 1 If the patient is decidedly toxic and unable to retain fluids and food by mouth nutrition and fluid balance of the body must be maintained by intravenous feedings Some have advocated in the early stages, particularly when there is constipation, that the gastro intestinal tract should be evacuated by means of saline cathartics and enemas The purging, however should not be debilitating Emptying the bladder should be carried out by catheterization 3 or 4 times a day or by furtrethonium (Furmethide) iodide subcutaneously in a dose of 1 2 to 2 5 mg for infancy to 4 years 2 0 to 3 0 mg for ages 5 to 9 years, and 2 5 to 5 mg for ages 10 to 19 years Care must be exercised in the use of furtrethonium Flushing and chilling can follow its use, and fainting may occur if the patient is in erect posture If a toxic reaction should develop, it can be quickly relieved by appropriate dosage of atropine sulfate

If cyanosis appears or the patient is very toxic oxygen therapy should be given For this purpose the cellophane mask is satisfactory

There is no specific chemotherapy for poliomyelitis The sulfonamides penicillin and streptomycin have been found to be of no benefit Phenolsulfazole is still under study, with recent reports being unfavorable The same is true of aureomycin Convalescent or adult serum

and the patient is responding satisfactorily, the dose should then be increased to 1 5 units per kilogram of body weight This dose should not be exceeded Obese patients should have the dose gradually increased in 0 2 unit increments until the optimum dose is found or 1 5 units per kilogram is reached

Since severe reactions can and do occur with curare therapy there should always be available for immediate use a syringe containing 0 5 mg of neostigmine (Prostigmine) and 0 6 mg of atropine After the curare has taken effect, usually about 45 minutes, the contracted muscles can be stretched through their normal range of motion All contracted muscles including those of the spine should be carefully manipulated and this routine followed until normal length is regained This therapy should combine the skills of a physiotherapist and one experienced in the use of curare Careful muscle surveys should be done and repeated until normal positioning is obtained Further reports on the use of these and possibly other similar drugs will be needed before the place of this form of treatment in the therapy of poliomyelitis can be accurately determined

The Abortive Phase The phase in which paralysis does not occur, may be difficult to recognize and is established principally by the spinal fluid findings and muscular tenderness and spasms With increased cell count in the spinal fluid poliomyelitis may be confused with benign lymphocytic choriomeningitis or with the Guillain Barre syndrome It seems wisest therefore if in doubt to treat such a case of poliomyelitis with prolonged bed rest sedation and heat Careful observation should be made for muscle tenderness and spasm with warm packs to these places or antispastic drugs given as recommended above Complete restoration of muscle function should be assured before the patient is allowed out of bed and before convalescence is carried out

The Paralytic Phase The same measures outlined for the pre paralytic stage of poliomyelitis should be continued through this stage of the disease Exercises both passive and active are to be limited during the acute paralytic phase and any motions and manipulations to be carried out are best done by a trained physiotherapist What is more important at this time is a critical evaluation of which muscles or groups of muscles are involved and to what extent paralysis has taken place No movement of muscles or muscle groups to the point of residual pain or fatigue should be allowed

Although the Kenny treatment recommends that no supports be used most agree that there should be some support of the effected parts against

water at the bedside wrung 2 or 3 times through a clothes wringer, applied promptly to an area and then covered with oiled silk and dry flannel The periodic application of moist woolen packs should be continued until all muscle tenderness and spasm have disappeared This may be for several days to several weeks, and the treatment should be continued through the paralytic stage if those symptoms persist

The use of drugs effective *against the* pain contraction, and spasm of muscles in poliomyelitis shows promise Mephenesin (Tolserol), benzazoline (Priscoline) hydrochloride and curare have been used with favorable results It seems well worth using one of these in the painful, early days of poliomyelitis especially if there is still fever Benzazoline (Priscoline) should be given *at first* by intramuscular injection, later by mouth dosage The dosage varies with the age of the patient, the amount to be given being determined by the appearance of flushing as evidence that an effective amount has been used The following plan of therapy is advised For patients aged 15 *years or older* begin with an intramuscular dose of 50 mg, if flushing results 50 mg every 3 or 4 hours, if no flushing results, add 12 5 mg every 3 or 4 hours until there is flushing, use this dose or the next *smaller* one as maintenance dosage until pain and muscle spasm subsides then shift to oral dosage using 12 5 mg per dose above the amount for the intramuscular route For patients aged 5 to 15 years begin with a dose *of* 37 5 mg increasing by 12 5 mg as just described For patients aged 1 to 5 years the initial dose should be 25 mg and the increment 12 5 mg For infants up to 1 year of age 10 mg in an elixir every 3 hours by day and every 4 hours by night is advised In all patients the dosage used must be large enough to produce flushing Benzazoline (Priscoline) has usually been continued for 10 to 15 days in the plan just outlined Nausea and vomiting not infrequently follow soon after a dose has been given if so, smaller doses should be tried These symptoms usually cease when the temperature has fallen to a normal level Occasionally there may be diarrhea Palpitation is not infrequent and sweating is common There may be a chill, calling for a warm blanket The use of the drug in patients with bulbar symptoms has not been effective in reducing the mortality rate but it can be used for patients in a respirator to lessen their pain Mephenesin (Tolserol) is also effective but its evanesent action limits its value Curare preparations have also been used and do give relief of spasm but their action is difficult to control Curare is given intramuscularly as Intocostrin in a dose of 0 9 units per kilogram of body weight every 8 hours for the first 3 doses If no reaction has occurred

corbic acid and 50 mg of thiamine chloride, 3 times a day Their use will do no harm In this phase particularly, penicillin 20 000 to 30 000 units of aqueous solution every 4 hours or 300 000 units of procaine penicillin in aqueous suspension may be very helpful in preventing a pneumonitis

Since the respirator is not satisfactorily effective in some patients with bulbar poliomyelitis and since its use may increase circulation deficiencies in many patients, some other means for control of respiration is desirable For this control there was recently introduced the so called electrophrenic respiration. This is applicable only when at least one vagal nerve is functioning for it consists in the rhythmic stimulation of the vagal nerve as a way to control respiratory movements It has seemed to be particularly effective in those patients with respiratory arrhythmia especially those with a Cheyne Stokes type of respiratory arrhythmia and can be used when the respirator has not been satisfactorily effective The place it may take in the management of the poliomyelitis patients with various respiratory difficulties can be determined only after it has been used on a large number of these patients

The Recovery Stage

This period extends from 3 to 6 months after the acute paralytic stage has subsided It is the stage in which carefully planned rehabilitation is to be started with as much emphasis on psychotherapy as on muscle function The patient and the family should be encouraged as far as it is possible to do with honesty for some degree of recovery is certain to take place Recent statistical analyses have shown that with good care 75 to 85 per cent of cases will show marked improvement or complete recovery About 10 to 20 per cent require the use of braces or aid from reconstructive surgery and only 2 to 5 per cent remain completely disabled A frank discussion to produce understanding in the patient and the relatives will go a long way to insure their co operation in the future course of treatment that may need to be carried out

Passive movement of muscles and graduated active exercises in which the patient is educated will help to bring about the mental orientation that is so useful in this stage Massage is to be kept at a minimum particularly if any muscle soreness or tenderness persists The muscle re education of the patient is to be increased slowly always short of the point of pain spasm or fatigue Many advocate the use of underwater

gravity and for weight bearing Casts should not be applied Splints, however, should not be used when they increase muscle spasm

With the onset of paralysis the physician and the attendant should be most alert to the development of bulbar signs and symptoms This is often manifested by difficulty in swallowing Difficulty with respiration is the symptom of importance, but a pure bulbar form seldom occurs Yet the differentiation is important, for all authorities are in agreement that, when respiratory difficulty is predominantly bulbar in origin, an artificial respirator is contraindicated A respirator under such circumstances is thought to force laryngeal and bronchial secretions into the lungs and at the same time to prevent the patient from expectorating such secretions naturally All that is usually required with the bulbar type of respiratory difficulty is the use of a mechanical aspirator, which may be needed without interruption 24 hours at a time, and postural drainage A few do use the respirator, however, advising elevation of the foot of the respirator 10 to 12 inches to provide postural drainage and to make aspiration of saliva and other secretions less likely Occasionally tracheotomy is life saving in these patients When patients recover from pure bulbar paralysis, the recovery is usually complete

Respiratory difficulty in anterior poliomyelitis is usually a combination of bulbar paralysis intercostal muscle paralysis from spinal involvement, and diaphragmatic disturbance The use of the respirator has been advocated principally where the chief involvement has been in the intercostal muscles of respiration, that is respiratory embarrassment of the spinal type. However with the introduction of the Sister Kenny treatment the opinion has become divided The Kenny group feels that a respirator should seldom if ever be used, that the same benefit may be derived by the application of the hot blankets to the intercostal muscles as well as elsewhere Those who have seen patients tided over with a respirator will not subscribe completely to such a point of view Since a respirator should not be used continuously but intermittently to allow as much natural breathing as possible, and since the hot packs are also to be used intermittently it seems wisest to apply both measures alternately in the spinal type of respiratory embarrassment Oxygen therapy may be given by nasal catheter as needed

With the patient in a respirator, feedings through a Levine tube, passed through the nose, may be carried out provided there is no regurgitation of stomach contents into the pharynx The other alternative is intravenous feedings with glucose, saline, and amino acid solutions Some have advocated the parenteral administration of 100 mg of as-

every ounce of possible strength Well supervised physical therapy should aim toward proper development of the strong and often unop posed normal muscles to prevent contractures and distortions Time should not be wasted on muscles fully paralyzed, but graduated exer cises to develop weakened muscles and to re educate the function of muscles remaining well are to be carried out diligently the end result to be striven for is rhythmic co ordinated movements of the part

The convalescent stage may go on for months even years for some muscles with improvement in strength and function Whereas previously 5 years used to be considered the outer limit of restoration of function, at the present time damage is considered to be more or less permanent after 18 months after which there remains the residual stage

The Residual Stage

In cases of poliomyelitis in which definite paralyses have occurred there is spontaneous complete, or nearly complete recovery in as many as 35 to 60 per cent In 20 per cent or less braces or reconstructive surgery are necessary in this stage of the disease The latter is necessary chiefly to correct deformities some of which will occur in spite of the best of earlier treatment These procedures fall entirely in the domain of the orthopedic surgeon the many technical operations of which will not be discussed here

Physical education, manual training sports games and so on are an integral part of this program along with vocational training to fit the crippled child for an independent useful and happy life

One word of caution is advisable in this stage Although every effort within reason should be made to bring about as complete recovery and rehabilitation as possible unnecessary length of hospitalization and pro longation of treatment is costly and economically unsound When pos sible therefore a therapist may visit the home or the person may be seen as an out patient at the hospital at intervals

Epidemiology and Prevention

Most of the investigation and advances in knowledge in poliomyelitis in the past few years has been along the line of epidemiology Although some progress has been made still there is too little known concerning the prevention of the disease Today it is considered that poliomyelitis

gravity and for weight bearing Casts should not be applied Splints, however, should not be used when they increase muscle spasm

With the onset of paralysis the physician and the attendant should be most alert to the development of bulbar signs and symptoms This is often manifested by difficulty in swallowing Difficulty with respiration is the symptom of importance, but a pure bulbar form seldom occurs Yet the differentiation is important, for all authorities are in agreement that, when respiratory difficulty is predominantly bulbar in origin, an artificial respirator is contraindicated A respirator under such circumstances is thought to force laryngeal and bronchial secretions into the lungs and at the same time to prevent the patient from expectorating such secretions naturally All that is usually required with the bulbar type of respiratory difficulty is the use of a mechanical aspirator, which may be needed without interruption 24 hours at a time, and postural drainage A few do use the respirator, however, advising elevation of the foot of the respirator 10 to 12 inches to provide postural drainage and to make aspiration of saliva and other secretions less likely Occasionally tracheotomy is life saving in these patients When patients recover from pure bulbar paralysis, the recovery is usually complete

Respiratory difficulty in anterior poliomyelitis is usually a combination of bulbar paralysis intercostal muscle paralysis from spinal involvement, and diaphragmatic disturbance The use of the respirator has been advocated principally where the chief involvement has been in the intercostal muscles of respiration, that is respiratory embarrassment of the spinal type However with the introduction of the Sister Kenny treatment the opinion has become divided The Kenny group feels that a respirator should seldom, if ever be used, that the same benefit may be derived by the application of the hot blankets to the intercostal muscles as well as elsewhere Those who have seen patients tided over with a respirator will not subscribe completely to such a point of view Since a respirator should not be used continuously but intermittently to allow as much natural breathing as possible, and since the hot packs are also to be used intermittently, it seems wisest to apply both measures alternately in the spinal type of respiratory embarrassment Oxygen therapy may be given by nasal catheter as needed

With the patient in a respirator feedings through a Levine tube, passed through the nose, may be carried out provided there is no regurgitation of stomach contents into the pharynx The other alternative is intravenous feedings with glucose, saline, and amino acid solutions Some have advocated the parenteral administration of 100 mg of as-

dehydration These require detailed attention and should be prevented if possible, if they do develop, they should be treated early and as thoroughly as possible Some patients instead of being lethargic are restless, have insomnia and may develop convulsions, they require effective sedation with drugs as described in Part 1 Drainage of spinal fluid by lumbar puncture may give relief from some of the restlessness and insomnia In few conditions is skilled meticulously careful, nursing care more needed Nutrition must be maintained and as soon as possible physical therapy muscle training, and psychotherapy started

Prophylaxis should include the usual precautions against the spread of infectious diseases with prevention of access of insects to the ill patient In time of epidemics protection of individuals against insects is advisable by modern methods of screening and the use of Chlorophenothane (DDT) and similar insecticides Contact with sick equine animals should be avoided Such animals should be isolated from human contact and if possible from insects Available evidence suggests the mosquito as the most probable insect transmitter of these diseases For the Eastern and Western equine type formalized chick embryo vaccine is useful in preventing the disease in animals Active immunization is possible against the St Louis type with inactivated virus vaccine Hyperimmune and convalescent serums have not been helpful

The serious sequelae of this group of diseases are the central nervous system disturbances, especially paralysis agitans or the parkinsonism group It is not known how during the acute phase of illness to prevent the subsequent development of these If they develop their management will be found described in the section on Paralysis Agitans

Lymphocytic Choriomeningitis

No specific therapy is available for this virus infection Supportive measures and repeated lumbar punctures are indicated Prophylaxis consists of excluding mice the natural reservoir for the disease from all possible contamination of food or living quarters The patient s urine should also be disinfected

Rabies

The aim in the treatment of rabies is to remove or destroy locally as much of the virus in the wound as possible to handle the offending

movement of the parts at this stage, to help the patient gain confidence as well, although this is not advocated by the Kenny group, on the basis that underwater movements have no counterpart in human movements on dry land In the Kenny method a warm bath may be given before educational procedures are carried out on a treatment table, or if there is sluggish circulation contrast douching of the parts with warm and cold water, then a warm bath followed by the treatment table may be carried out

With neurological recovery muscle tone and power return rather rapidly and at this point attention to bones, joint function, and nutritional state should be continued as well By this time the infectiousness of the disease has passed and the patient may be moved, some advocate removal to a convalescent home or crippled children s institution, if necessary, where the most definitive treatment can be carried out by trained workers Many consider the psychological benefits of being with other crippled children, who are making the same struggle to recover and adjust, as important as the mechanical therapy of restoration of muscle function

Treatment from now on should be guided largely by repeated muscle checks compared to the original observations and by the speed of recovery Occupational therapy and regular school sessions are very important to institute at this time, since convalescence may be quite prolonged

The Convalescent Stage

This becomes the quiescent stage in which various types of treatment are to be carried out to rehabilitate the patient to a life as useful and happy as possible The aim in treatment at this stage should be to teach the patient the most efficient use of the muscles he is capable of moving, co ordination and balance are of far greater importance than muscle strength alone In this stage attempts are made to correct deformities, the fact that prevention of deformity is much easier than correction of deformity explains why the principles of treatment outlined for the early stages of the disease are so important

Braces to the lower extremities and splints and cuffs to the upper extremities are often used fortunately many times as a temporary expedient, to allow early ambulation and to prevent deformity For paralyses of the trunk, back, and abdominal muscles the best therapy is properly supported recumbency in bed to aid the patient in regaining

dehydration. These require detailed attention and should be prevented if possible; if they do develop, they should be treated early and as thoroughly as possible. Some patients instead of being lethargic, are restless, have insomnia and may develop convulsions; they require effective sedation with drugs as described in Part 1. Drainage of spinal fluid by lumbar puncture may give relief from some of the restlessness and insomnia. In few conditions is skilled meticulously careful nursing care more needed. Nutrition must be maintained and, as soon as possible, physical therapy, muscle training and psychotherapy started.

Prophylaxis should include the usual precautions against the spread of infectious diseases with prevention of access of insects to the ill patient. *In time of epidemics protection of individuals against insects is advis*able by modern methods of screening and the use of Chlorophenothane (DDT) and similar insecticides. Contact with sick equine animals should be avoided. Such animals should be isolated from human contact and if possible from insects. Available evidence suggests the mosquito as the most probable insect transmitter of these diseases. For the Eastern and Western equine type formalized chick embryo vaccine is useful in preventing the disease in animals. Active immunization is possible against the St. Louis type with inactivated virus vaccine. Hyperimmune and convalescent serums have not been helpful.

The serious sequelae of this group of diseases are the central nervous system disturbances, especially paralysis agitans or the parkinsonism group. It is not known how during the acute phase of illness to prevent the subsequent development of these. If they develop their management will be found described in the section on Paralysis Agitans.

Lymphocytic Choriomeningitis

No specific therapy is available for this virus infection. Supportive measures and repeated lumbar punctures are indicated. Prophylaxis consists of excluding mice, the natural reservoir for the disease, from all possible contamination of food or living quarters. The patient's urine *should also be disinfected.*

Rabies

The aim in the treatment of rabies is to remove or destroy locally as much of the virus in the wound as possible, to handle the offending

is a person-to-person disease with transmission of the known virus from the intestinal tract of one to the intestinal tract of another It is felt that this explains the presence of virus in the pharynx, for the pharynx is the entrance to the gastro intestinal tract

The exact mode of transmission from one person to another, however, is not known Sewage in water contaminated milk, and certain species of flies have contained the virus, but attempts to isolate consistently the virus from mice rats muskrats, chickens, cows, hogs, horses, cats and numerous insects other than flies have been unsuccessful

From what is known the measures of prevention are few and include (1) the avoidance of fatigue in poliomyelitis season to diminish neuromuscular susceptibility (2) careful personal hygiene (3) strict avoidance of water or milk that is possibly contaminated, (4) riddance of flies with Chlorophenothane (DDT) although the latter has no effect on the virus of poliomyelitis and thorough washing of whatever is to be eaten uncooked, (5) avoidance of bathing or swimming in water frequented by others (6) avoidance of operations on tonsils and adenoids during an epidemic (tonsillectomy in such circumstances may give rise to the severest form of the disease the bulbar type of poliomyelitis (7) possible avoidance of various immunizing procedures during the polio myelitis season such as diphtheria and tetanus toxoid injections, and (8) avoidance of intimate association such as hand shaking, kissing and use of common eating utensils and towels with members of a family in which poliomyelitis has occurred within three weeks, even if the patient has been removed to a hospital There is recent evidence to indicate that gamma globulin may be helpful in preventing the disease and in reducing the incidence of paralysis Methods of active immunization with attenuated virus have been developed which are effective in protecting animals It may not be long before both passive and active methods of immunization will be available to man

Epidemic Encephalitis Encephalomyelitides

At present there is no known specific therapy effective in the treatment of this group of diseases Consequently treatment is entirely symptomatic and should be as described in Part 1 Since many of these patients are lethargic various developments are likely such as retention of urine, failure of bowels to move with possible fecal impaction, development of bed sores, inability or refusal to swallow needed nutrition, and

and there were no symptoms of rabies its brain nevertheless should be sent to the laboratory Laboratory studies have shown that sections taken from the Gasserian ganglion are much more likely, especially in early cases to show Negri bodies Consequently studies of the ganglion should be made on all animals suspected of having rabies

In most instances there will be no evidences of rabies at the time of the bite consequently the dog should be captured confined and observed Opinions differ somewhat in details but most agree that, if the animal has shown no evidences of rabies within 10 and certainly within 14 days the diagnosis of rabies may be dismissed If however the animal develops the symptoms within that period of time, it should then be killed and the brain sent to the laboratory for study to confirm the diagnosis If there is good reason for doubt the animal should be killed after 14 days and the necessary laboratory studies of its brain made If the animal cannot be confined and observed some advocate that it should be regarded as rabid and preventive inoculations carried out

Preventive Immunization

Because statistical evidence has shown that only 15 to 25 per cent of individuals bitten by rabid dogs and possibly only 40 to 50 per cent bitten by other animals actually develop rabies the physician is often reluctant to use preventive immunization on less evidence than the actual proof of rabies in the offending animal This is so because of the knowledge that vaccine treatment can do harm in the form of pareses paralysis and polyneuritis in an individual in whom rabies might never have developed

Yet the disease is so serious that if there is reasonable doubt one cannot afford to take a chance by not giving treatment When the offending animal has been demonstrated to be rabid one must vaccinate Vaccination with attenuated virus has proved successful The Pasteur method of using dried spinal cord attenuated virus which caused quite a few reactions when it was in use has been largely replaced by newer preparations nearly devoid of reactions There are 3 forms of vaccine (1) phenol killed and chloroform killed virus (Semple method) (2) *ultra violet killed virus (Rabies Iradozen) and (3) attenuated virus* (Harris method) All are effective The method of administration and dosage directions are given in the pharmaceutical package

The dosage and the frequency of injections are dependent also upon

animal properly and then to give preventive immunization to the individual so that the disease will not develop Once the clinical picture develops in either animal or man, the subject will die, for there is no known cure

Local Treatment

Since it has been shown that the virus of rabies travels centralward very slowly along nerve pathways and not in the blood stream or lymphatics and since vaccination treatment has been found to protect against only a limited amount of the virus, as much of the offending agent should be removed or destroyed at the site of inoculation as possible Although thorough cleansing with soap and water is probably as effective as chemical destruction many prefer to use the time tested application of phenol solution (carbolic acid) or fuming nitric acid In the case of laceration, the wound should be allowed to bleed rather freely and should then be thoroughly cleaned with soap and water and 3 per cent hydrogen peroxide applied to clean further and remove any particulate matter If the wound is a deep puncture, these measures, plus the application of phenol or nitric acid lead to greater safety When either of these highly irritating substances is used, the skin surrounding the wound should be covered with petrolatum for protection, then the chemical is applied directly into the wound If the wound is a puncture it may be incised to produce free bleeding, and then the measures just described carried out After either phenol or nitric acid has been applied, the wound should be washed with a saturated solution of sodium bicarbonate followed by 95 per cent alcohol The wound should then be left open, not sutured

The Animal This is most commonly the dog, but it may also be the fox wolf cat, horse cow, skunk or vampire bat Most warm blooded animals are susceptible In the care of the animal, too often ill judgment is used, the animal is captured killed and frequently nothing is gained thereby It should be remembered in the case of the dog that the saliva is infectious for only 4 to 6 days before symptoms develop in the animal, and that the diagnostic Negri bodies of the central nervous system are late in their appearance and the following course of action should be followed If there is definite evidence clinically at the time of the bite that the dog has rabies the animal should be killed promptly and the brain sent to a qualified laboratory for proper study Even if the animal unfortunately has been killed at the time of the bite

sedation with them should be pushed Spasms may be controlled by intravenous pentobarbital (Nembutal), 0 3 to 0 6 gm or phenobarbital, 0 3 to 0 6 gm It may be necessary to repeat the dose several times a day Intravenous saline and 5 or 10 per cent dextrose are helpful in maintaining hydration and giving nourishment

Prophylaxis

In the dog prophylaxis may be carried out by the subcutaneous injection of 5 cc of chloroform treated vaccine It has been proved in certain countries that muzzling of all dogs will eradicate the disease If all stray dogs were impounded rabies would be greatly decreased

Prophylaxis in the human subject is discussed under local treatment and under preventive immunization

BIBLIOGRAPHY

Poliomyelitis

1 Amer Orthopedic Assn Infantile Paralysis or Acute Poliomyelitis A brief Primer of the Disease and Its Treatment *Jour Amer Med Assoc* 1946 CXXXI p 1411

2 CUNNING D S Poliomyelitis Tonsillectomy Survey 1948 *Laryngoscope*, 1949 LIX p 441

3 RANSCHOFF N S The Treatment of Anterior Poliomyelitis *Med Clin No Amer* March 1950 p 553

4 SABIN A B Transmission of the Poliomyelitis Virus *J Pediat* 1951 XXXIX p 519

5 VOGEL E Medical Progress Recognition Treatment and Control of Poliomyelitis (Prize Essay) *N E J Med*, 1950 CCXLII p 899

6 WISHART D E S Rhinology in Children Resume of and Comments on Literature for 1948 *Laryngoscope* 1949 LIX p 929

7 GEAR J Immunity to Poliomyelitis *Ann Int Med*, 1952 XXXVII p 1

Rabies

1 TIERKEL E S GRAVES L M TUGGLE H G and WADLEY S L Effective Control of Outbreak of Rabies in Memphis and Shelby County Tennessee *Am J Pub Health*, 1950 XL p 1084

the site of the bite, and are much more urgent when the bite has been about the face, neck head, and bare extremities because they do not have the protection afforded when the bite has been through clothing Other factors include the interval of time between the injury and the beginning of inoculations and the age of the patient, larger and more frequent doses are required in children than in adults

The usual course of inoculations is a daily injection for 14 days In mild cases, or where reactions are occurring, 7 days may suffice In severe cases it may have to be prolonged to 28 days In instances of large wounds or where vaccination has been started late, it may be best to give 2 injections a day for the first 7 days, than 1 injection daily

The duration of immunity produced by such vaccination is not definitely known It is thought to be about 1 year If there is a re exposure more than 3 or 4 months after the immunization, it should be treated by a second course of vaccine injections

It is thought that the reactions to vaccination particularly polyneuritis, may be on an allergic basis owing to sensitivity of the individual to rabbit s brain and cord rather than to the vaccine For that reason it may be advisable to skin test the individual with the vaccine to be used, and to desensitize the patient found to be sensitive as rapidly as possible, before giving the full course of inoculations Diphenhydramine (Benadryl) hydrochloride, 50 to 100 mg 3 times a day, relieves pruritis and urticaria of the local sensitivity reactions

Dogs may be immunized by a single subcutaneous injection of 5 cc of chloroform treated vaccine The duration of such protection is not known but a program of community immunization of dogs effectively reduces the incidence of the disease

The Treatment of an Acute Attack of Rabies

Rabies is invariably fatal The treatment is entirely symptomatic, palliative against the irritability, sleeplessness maniacal symptoms throat spasms, and convulsions The patient should be kept as quiet as possible in a darkened room Local application of anesthetics such as nupercaine lozenges (Nuporals) butacaine (Butyn) sulfate, 2 per cent or cocaine hydrochloride, 4 per cent, to the throat is useful to delay the spasms and pain in the throat, so the patient may be able to swallow nourishing drinks and perhaps soft foods The use of morphine should be avoided since it may increase excitement The barbiturates are valuable and

Mumps

No specific measures exist for the treatment of mumps, and fortunately the disease usually runs a benign course In certain circumstances it may be wise to prevent the development of mumps in exposed individuals Convalescent blood serum in a dose of 20 cc for children and 40 cc for adults is often effective It is doubtful whether this serum is of much value in the treatment of the established disease It is possible however that concentrated gamma globulin prepared from convalescent serum is of value in preventing orchitis Immediate bed rest continued until the fever and parotid swelling have disappeared isolation a liquid to soft diet analgesics and sedatives are advised Pain from the swollen glands in the early stages of the disease is ameliorated by the use of hot compresses or ice packs Most patients prefer the latter The mouth should be kept as clean as possible A warm mouthwash of Compound Sodium Borate Solution N F (Dobell's solution) is helpful If stomatitis develops aureomycin troches may prevent much discomfort In the presence of delirium or marked restlessness phenobarbital is of value In cases with high fever an ice cap on the head is restful Male adults should receive 1 0 mg of diethylstilbesterol U S P twice daily as a prophylaxis against orchitis

In adults ochitis or oophoritis may appear and be most painful In such cases the patient should avoid activity and in the male the testicles should be protected by cotton wool and supported to avoid dependency Care must be taken to avoid pressure or trauma to the organs and cold applications should be administered in such fashion as to avoid exerting any pressure or in any way inhibiting or interfering with the circulation For orchitis diethylstilbesterol U S P in a dose of 2 0 mg 3 times a day for 5 to 7 days is usually effective and in a period of 24 to 48 hours relief from pain and swelling commences

In the severely ill patient with marked constitutional symptoms in whom rapid testicular swelling appears and pain is pronounced especially when one testicle is just developing orchitis while the other is already involved and diethylstilbesterol is not affording relief, the scrotum should be opened under local anesthesia and the tunica vaginalis should be incised first, then the tunica albuginea if relief is not obtained

Prevention Virus vaccines show promise but are not generally available as yet The administration of diethylstilbesterol as outlined above is beneficial in the prevention as well as in the treatment of orchitis

CHAPTER XIV

OTHER VIRAL DISEASES

Infectious Mononucleosis

The treatment of this usually benign but occasionally severe disease is still symptomatic Further studies have not supported the reported successes with antibiotic therapy, although it may make the patient feel better without having any influence on the course of the disease Isolation, bed rest and adequate fluid intake are essential The diet should be high in protein and carbohydrates but moderate to low in fat and should be supplemented with vitamins especially B complex Calorie intake should be high and as much as 4000 cc of fluid a day should be given If laboratory studies show signs of hepatitis, the same dietary regime as described for Infectious Heptatitis is indicated, and bed rest should be continued until all signs of hepatitis have disappeared

Acetylsalicylic acid, 0 6 gm every 4 hours or methadone, 5 to 10 mg 3 times a day usually controls the pain If there is tonsillitis, Vincent's infection, or any other secondary complication of an infectious nature, aureomycin or other antibiotic depending on the sensitivity of the organism, is indicated Tonsillitis and Vincent's angina should also receive the treatment prescribed for them

Convalescent serum may be of value This serum, collected from convalescent patients 1 to 2 weeks after they are afebrile, is given intravenously in a total dose ranging from 60 to 300 cc The majority of patients require between 100 to 200 cc The total dose may be divided into two injections and administered intravenously

Scarlet fever convalescent serum may be helpful also especially in patients with severe throat involvement An intravenous dose of 100 cc may give marked relief

Prophylaxis Strict isolation of cases especially in epidemics, avoidance of close contact, and possibly the use of air sterilizing sprays and ultraviolet lights will help to control the spread of this disease The usual precautions against the spread of viral diseases should also be observed

be combined with aureomycin terramycin, chloramphenicol, or sulfadiazine to secure maximal results

Antimony in the form of lithium antimony thiomalate (Anthiomaline) containing 16 per cent antimony has had considerable trial with results in some cases equal to those with sulfonamides Anthiomaline is to be administered intramuscularly in aqueous solution 0 1 to 0 3 gm 2 to 3 times a week for a total of 12 to 0 injections Such a course may be repeated after a rest period of a few weeks

The Chronic Stage

Even in the late stages with scar tissue formation, one of the antibiotics will be useful particularly for secondary infection It will lessen the amount of discharge and may allow for spontaneous healing which occurs in a certain number of patients with lymphogranuloma venereum

Vaccinotherapy in ascending subcutaneous doses at 5 day to weekly intervals beginning with 0 05 cc and increasing 0 01 cc as indicated to a maximum dosage of 1 0 cc may prove useful in chronic cases Vaccinotherapy combined with an antibiotic may prove of considerable help in chronic cases and in those with complicating rectal stricture

The complications of the chronic stage are chiefly rectal stricture perirectal abscess and fistula in ano Rectal stricture is much more common in the female than in the male In either sex prolonged gentle rectal dilatation, preferably carried out manually at weekly intervals is advisable Colostomy should not be performed unless manual dilatation has failed Surgical incision and drainage is the treatment to be used for perirectal abscess A fistula in-ano should be excised whenever that is possible

Local diathermy and intensive estrogenic therapy may soften strictures but the results are not uniformly good

Coincidental syphilis and gonorrhea should be tested for and if found treated promptly as outlined in the sections on Syphilis and Gonorrhea

Herpes Simplex Herpes Febrilis

Very often no treatment is needed, for the vesicles quickly dry up and in their course cause very little discomfort This is often true of locations other than on the cornea where the herpetic lesions may cause scarring with subsequent opacity of the cornea may be extremely painful or

since it temporarily returns the testicle to the prepuberal state, in which period orchitis is less serious

Lymphogranuloma Venereum

The treatment of lymphogranuloma venereum consists of management during (1) the acute stage and (2) the chronic stage

Acute Stage

Bed rest is a very important measure, along with nourishing diet, proper fluid balance and acetylsalicylic acid, 0 3 to 0 6 gm, for discomfort Aureomycin, 1 0 gm orally 4 times a day, should be given for the first day and then 0 5 gm orally 4 times a day as long as improvement continues On the fourth or fifth day after beginning aureomycin therapy, discharge and bleeding from sinuses or rectum will usually be controlled or markedly reduced and the enlarged lymph nodes will be reduced in size The patient with proctitis may also show increase in size of stool diameter If the early case is resistant to aureomycin, or if aureomycin causes toxic symptoms terramycin in an initial dose of 1 gm 4 times a day, followed by 0 5 gm 4 times a day by mouth, should be tried Chloramphenicol is also effective in the same dosage Sulfonamides are for the most part being replaced by the less toxic and more effective antibiotics If the antibiotics are not available, then sulfadiazine 1 0 gm 5 times a day, should be given The usual precautions taken during sulfonamide therapy must be observed The sulfonamide should be administered for at least 20 days frequently much longer If very prolonged administration becomes necessary, it is well to discontinue it for a rest period of a week or two

For a secondary infection with pyogenic organisms that is not controlled by the antibiotics or sulfonamides listed above, penicillin or streptomycin is advised Incision or excision of lymph nodes should not be carried out, as it does not promote healing and may increase the later developing scar tissue with resulting elephantiasis fluctuant buboes should be aspirated, especially if perforation seems imminent

If these antibacterials fail the intradermal injection of Frei antigen, 0 1 to 0 2 cc every other day for 8 to 10 doses should be tried This treatment seems to be effective also in the stage of lymph node involvement For more chronic forms of the disease, vaccine therapy should

istered by intramuscular injection The solution is given in doses of 1 3 cc (1 ampule) daily for from 4 to 8 or more injections Pain is relieved quite promptly if the injections are given early in the course of the affliction

At first aureomycin and chloramphenicol were thought to hold promise in the treatment of herpes zoster but later better controlled studies have shown no benefit over and above symptomatic measures Aureomycin and terramycin 500 mg as an initial dose followed by 250 mg every 4 hours, may be useful in combatting secondary infection although control studies have shown also that with symptomatic treatment alone secondary infection is quite uncommon with herpes

There are several procedures that have been found to be of value in the management of herpes zoster and which give varying degrees of relief in individual cases these should be tried in case aureomycin is ineffective in a given case The pain which may precede accompany or follow the appearance of the vesicles may present a serious problem and its control may tax the ingenuity of the physician Simple analgesics such as acetylsalicylic acid 0 6 gm repeated at 4 hour intervals are indicated in the beginning If this does not give relief it is wise to try a combination of acetylsalicylic acid phenacetin and caffeine Barbit urate sedation when combined with analgesics often helps in pain control Codeine may be added also if relief is still not obtained Finally it may be necessary to resort to meperidine (Demerol) hydrochloride 50 to 100 mg, methadone 5 to 10 mg or morphine sulfate 8 to 15 mg Care must be taken to prevent addiction to merperidine methadone and morphine by using them as briefly as possible and by resorting to the simpler analgesics as much as possible Procaine or alcohol block of the appropriate sympathetic ganglia may give marked relief when properly done by one skilled in the technique Cobra venom intramuscularly in a dose of 1 0 cc daily for 2 or 3 days until the pain is relieved and then 1 0 cc every other day or at longer intervals as required may be of some assistance X ray therapy over the spinal ganglia in a dose of 00 to .50 roentgens daily is worth trying if pain persists after these other treatments have been used Surgical section of involved nerve roots has been used for otherwise intractable pain but not with great success

The eruption should be protected by a soft cotton dresssing to keep the vesicles in an intact state Skin irritation pruritis and pain respond well to locally applied calomine lotion U S P phenolated calomine lotion N F ointments containing ethyl aminobenzoate U S P Benzo cain 5 per cent in white ointment 95 per cent or the 10 per cent water

since it temporarily returns the testicle to the prepuberal state, in which period orchitis is less serious

Lymphogranuloma Venereum

The treatment of lymphogranuloma venereum consists of management during (1) the acute stage and (2) the chronic stage

Acute Stage

Bed rest is a very important measure, along with nourishing diet, proper fluid balance and acetylsalicylic acid, 0 3 to 0 6 gm, for discomfort Aureomycin, 1 0 gm orally 4 times a day, should be given for the first day and then 0 5 gm orally 4 times a day as long as improvement continues On the fourth or fifth day after beginning aureomycin therapy, discharge and bleeding from sinuses or rectum will usually be controlled or markedly reduced and the enlarged lymph nodes will be reduced in size The patient with proctitis may also show increase in size of stool diameter If the early case is resistant to aureomycin, or if aureomycin causes toxic symptoms, terramycin in an initial dose of 1 gm 4 times a day, followed by 0 5 gm 4 times a day by mouth, should be tried Chloramphenicol is also effective in the same dosage Sulfonamides are for the most part being replaced by the less toxic and more effective antibiotics If the antibiotics are not available then sulfadiazine, 1 0 gm 5 times a day, should be given The usual precautions taken during sulfonamide therapy must be observed The sulfonamide should be administered for at least 20 days, frequently much longer If very prolonged administration becomes necessary, it is well to discontinue it for a rest period of a week or two

For a secondary infection with pyogenic organisms that is not controlled by the antibiotics or sulfonamides listed above, penicillin or streptomycin is advised Incision or excision of lymph nodes should not be carried out, as it does not promote healing and may increase the later developing scar tissue with resulting elephantiasis, fluctuant buboes should be aspirated, especially if perforation seems imminent

If these antibacterials fail the intradermal injection of Frei antigen, 0 1 to 0 2 cc every other day for 8 to 10 doses should be tried This treatment seems to be effective also in the stage of lymph node involvement For more chronic forms of the disease, vaccine therapy should

Bed rest instituted promptly at the first appearance of hepatitis is most beneficial The earlier complete bed rest is commenced the better Exercise or too much activity can have a deleterious effect producing a more serious infection prolonging the course of the illness, and causing a relapse if begun too early or too vigorously during convalescence Continued activity may cause a chronic recurrent hepatitis Bathroom privileges are permissible except for the seriously ill Bed rest should be maintained on the average from 3 to 6 weeks or until at least 1 week after anorexia diarrhea, fatigue headaches lassitude fever and liver tenderness or enlargement have disappeared Then if the tests for liver function — such as the bromsulphalein, thymol turbidity cephalin flocculation or albumin globulin ratio — and the urinary excretion of urobilinogen have shown a definite trend toward normal limited activity may be allowed and gradually increased over a period of 7 to 10 days During this period if there is any recurrence of right upper quadrant distress or enlargement or tenderness of the liver or if laboratory tests show unfavorable trend complete bed rest should be resumed promptly Increased tolerance for activity is a real test of recovery

Diet

A diet high in carbohydrate and protein with sufficient fat to make it palatable is advised The protein moiety should be high in the essential amino acid methionine and the 100 to 150 gm taken daily should include large amounts of cottage cheese and skimmed milk The carbohydrate should be easily digestible with as much as 350 to 500 gm made up in large part of sweetened drinks which supply adequate fluids as well If the patient is extremely ill and has severe anorexia nausea or vomiting it is necessary to supply nutrition and fluids parenterally Sufficient physiological salt solution to which 5 or 10 per cent glucose has been added should be given to insure a daily urinary output of at least 1500 cc Should parenteral therapy be required for more than 2 or 3 days 5 per cent protein hydrolysate or 2 units of plasma should be added to the parenteral solution If there is anemia whole blood transfusions should be given Patients with decreased serum albumin receive distinct benefit from the daily administration of 50 gm of human plasma albumin Parenteral human albumin is useful particularly in the treatment of nausea and vomiting Unfortunately the supply is limited and the cost nearly prohibitive Whole blood transfusions or plasma are a

may cause secondary infection with resulting panophthalmitis, treatment of herpes of the cornea should be under the direction of a competent ophthalmologist If the lesions are situated elsewhere than on the cornea, the application of benzylkonium (Zephiran) chloride, 1 1000, to the vesicles is helpful When they are numerous on the mucosa of the mouth, a condition called follicular, vesicular, or herpetic stomatitis, cleaning the mouth with alkaline aromatic solution N F or compound sodium borate solution N F [Dobell s solution], as a mouthwash, is useful in maintaining oral hygiene When the herpetic lesions cause severe pain and prevent proper nourishment lozenges of nupercaine (Nuporals) rinsing the mouth with a 1 per cent solution of tetracaine (Pontocaine) hydrochloride, or cocaine hydrochloride, 4 per cent, gives sufficient relief to permit the ingestion of food Antibiotic therapy may be required to control secondary infections Aureomycin troches or, in the presence of severe involvement, in the usual dosage are recommended Tripelennamine (Pyribenzamine) hydrochloride, 50 mg by mouth every 6 hours, or diphenhydramine (Benadryl) hydrochloride in the same dosage will help to decrease itching and burning

A solution of Protamide, as described under Herpes Zoster, 1 3 cc intramuscularly daily for 4 to 8 or more injections, is a newer form of therapy that is showing promise, particularly for pain

If herpes simplex is recurrent, repeated vaccinations once every week for 6 or 8 weeks with smallpox vaccine will help prevent recurrence Herpes simplex especially on the lips and in the mouth, often accompanies various infectious diseases

Rarely, the virus of herpes simplex causes encephalitis or even more rarely, meningitis these should be treated as described under Encephalitis and Encephalomyelitis

There is no effective prophylaxis of herpes simplex

Herpes Zoster

As yet there is no specific curative measure for this virus infection Fortunately most cases are mild and self-limiting, with a duration of from 10 to 30 days, and respond readily to simple therapy The relationship of this virus to the virus of chickenpox has been postulated, but no definite proof has been worked out

Recently introduced for the treatment of herpes zoster is a colloidal solution of denatured proteolytic enzyme (Protamide), to be admin-

the return of appetite for the morning meal *Activity should be permitted gradually* One hour out of bed morning and afternoon of the first 2 or 3 days is recommended and this can be increased to 2 hours during the next 2 or 3 days Ambulation may then be undertaken but *the patient should receive 2 to 4 hours of bed rest during the day for* the next week Normal activities may be resumed gradually Frequent careful laboratory checks should be made and at the first sign of any increased liver impairment activity should be discontinued and further *rest instituted*

Prevention

The virus of the endemic and epidemic form of infectious hepatitis is spread in contaminated water and food and through contact with patients and carriers

Control consists of careful water purification prevention of food contamination destruction of flies avoidance of spread from infected patients, and the institution of strict sanitary measures

Patients with the disease should be under precautions against spreading infection and dishes linen excreta, garbage and all things with which they come in contact should be treated as described under Typhoid Fever

Individuals coming into contact with the patient should wear caps masks and gowns After contact with the patient or with articles that have been in contact with the patient the hands should be washed thoroughly with soap and running water and then rinsed carefully to remove all soap They should then be soaked in 1 1000 tincture of benzylkonium (Zephiran) chloride Instruments in contact with the patient should be soaked in a 1 1000 solution of benzylkonium (Zephiran) chloride

Infection in persons exposed to this virus can be prevented by the intramuscular injection of 0 06 to 0 12 cc per pound of body weight *of gamma globulin during the incubation period and up to 6 days before* onset of the disease One injection affords protection for from 6 to 8 weeks

Homologous serum virus is spread by the therapeutic use of homologous plasma or serum blood transfusions or through the use of improperly sterilized syringes or needles that have been in contact with infected material Since there are many carriers of the virus any serum

soluble benzocaine jelly (Anaesthesin) For painful lesions involving the eye, an ointment containing 1 per cent butacaine (Butyn) sulfate is recommended If the vesicles are broken or if there are signs of infection a 3 per cent aureomycin ointment should be applied, except in the eye where the 0 1 per cent ointment should be used, if the skin area is moist and an application of ointment would be unsatisfactory, the area should be dusted with zinc stearate to which aureomycin has been added

Many therapeutic methods have been reported but none is very effective Still they should be tried on patients not responding to the measures given above Some attacks are aborted by one of the following methods of treatment pituitrin 0 5 to 1 0 cc given at 24-hour intervals, sodium iodide given intravenously in a dose of 10 cc of a 20 per cent solution on the first, second fourth, and seventh days, and thiamine chloride in a dose of 100 mg daily potentiated with neostigmine (Prostigmine) methylsulfate 1 cc of a 1 2000 solution, given subcutaneously in the involved area at intervals of 2 to 4 days for 4 injections In an occasional case diphtheria antitoxin has proved helpful, as have the newer antihistaminic drugs diphenhydramine (Benadryl) hydrochloride or tripelennamine (Pyribenzamine) hydrochloride in doses of 25 to 100 mg 3 times a day

In the ophthalmic form care must be taken to prevent damage to the eye Boric acid eyewashes eye shields aureomycin ointment ophthalmic and a 1 per cent butacaine (Butyn) sulfate ointment are of value Convalescent serum taken from patients who have had herpes zoster previously shows some promise in the treatment of ophthalmic zoster

One attack usually confers immunity The pain however, may persist for many weeks after the initial lesion has completely healed and may present a serious problem Unrelieved severely painful cases have resulted in suicide Adequate control of pain by analgesics reassurance, and in the depressed cases judicious use of amphetamine (Benzedrine) sulfate as a component of the analgesic or alone are recommended

Viral Hepatitis

The essential features of the treatment of viral hepatitis whether endemic epidemic or homologous serum in type consist of adequate bed rest proper diet, and the avoidance of further liver damage Up to the present time no specific drug therapy for this form of hepatitis has been developed

additions of food items described in the typhoid diets Up to the present antibiotics have not proved helpful

Anemia should be treated with ferrous gluconate 1 to 2 gm daily as soon as the patient can tolerate iron Occasionally liver extract is helpful in a dose of 1 0 cc 2 or 3 times a week for a month Convalescence should be gradual and activity regulated carefully A long period of convalescence is usually necessary

Prophylaxis

Those in possible contact with yellow fever infected mosquitoes and those traveling in or through endemic areas should be vaccinated with an avirulent strain of yellow fever virus such as 17D at least 15 days before exposure Yellow fever is endemic in Africa and South America near the equator It may extend as far north as 20° and to 30° *south A dose of 0 5 cc of a freshly (within 1 hour) diluted* vaccine (1 10) is given subcutaneously to both children and adults This is contraindicated in the presence of allergy to eggs and should be avoided if there is a concurrent virus infection or smallpox vaccination Immunity lasts approximately 4 years Booster injections of 0 5 cc should be given every 4 years as necessary In the presence of an epidemic an emergency booster dose of 0 5 cc is advisable Individuals should be protected from the mosquito vector

Dengue

At present no specific treatment exists for this disease Prompt recovery is the rule

Elimination of mosquito contact, bed rest, a palatable light diet and avoidance of exertion are advised Sulfonamides and antibiotics are not effective Acetylsalicylic acid in 0 6 to 1 0 gm doses every 4 to 6 hours will lessen bone pains Analgesics such as morphine codeine meperidine (Demerol) hydrochloride, or methadone are indicated for the severe pains The effects of high fever can be ameliorated by hydrotherapy An ice bag applied to the head is helpful Intravenous fluids should be given if dehydration develops Shielding the eyes from light is helpful in eliminating the post orbital pain The post infection depression may be severe and require reassurance and occasionally it is

reasonably effective substitute for albumin and can be given in place of it

Adequate amounts of vitamins, especially of the B complex, should be given if there is evidence of a prior lack or indications of deficiency Oral or, when indicated parenteral administration supplying approximately thiamine hydrochloride 10 mg, riboflavin 5 mg, niacinamide 50 mg pyridoxine hydrochloride 5 mg sodium pantothenate 5 mg, and ascorbic acid 100 mg once or twice a day should supply the usual vitamin lack In chronic or long continued infections with jaundice, diarrhea and vomiting it is necessary to supply fat soluble vitamins as well A daily oral dose of vitamin A 30,000 I U, and vitamin D, 3000 I U, is sufficint These cases should also receive vitamin K, 2 to 5 mg intramuscularly daily

Methionine, 4 to 8 gm, or choline dihydrogen citrate, 2 to 3 gm daily by mouth, may be of benefit to those patients with chronic severe infections who are not receiving adequate amounts of protein or who are not responding to therapy If these substances are not well tolerated, the nausea and anorexia produced by them may offset any real benefit derived

Intravenous crude liver extracts 5 cc daily are helpful in stimulating appetite and supplying essential B complex vitamins

Avoidance of all possible factors that might cause liver trauma, such as intercurrent infections surgical procedures anesthetics, alcohol and drugs detoxified by the liver is advised Morphine and the barbiturates are not well tolerated and are prone to give prolonged and exaggerated effects The antibiotics rather than the sulfonamides should be employed in the treatment of intercurrent infections since the sulfonamides are capable of damaging the liver further Aureomycin and some of the other antibiotics have shown no real effect on the clinical course of viral hepatitis There is even a suggestion that at times aureomycin may be harmful

On the other hand with the presence of fever, leukocytosis, and increased erythrocyte sedimentation rate terramycin may be helpful It is given in doses of 0 5 to 1 0 gm every 6 to 8 hours by mouth or 1 0 gm daily intravenously in divided doses at 12 hour intervals For intravenous medication the drug should be dissolved in 5 per cent dextrose solution or physiological saline Each dose should be dissolved in at least 100 cc of the solution chosen and run into the vein slowly at a rate of no more than 100 cc in 5 minutes The terramycin should be continued for 10 to 14 days

As improvement occurs an excellent sign of beginning recovery is

There is some evidence that aureomycin by mouth in an initial dose of 2 0 gm followed by 0 5 to 1 0 gm every 4 hours is effective against the causative organism It is worthy of trial Methadone 5 to 10 mg, meperidine, 50 to 100 mg, either parenterally or dissolved in fruit juice will help relieve the painful cramps Occasionally morphine sulfate hypodermically 8 to 15 mg may be needed Tablets of aspirin 0 3 gm every 3 to 4 hours are comforting Heat applied to the abdomen is also useful and soothing It is doubtful if sufficient benefit is obtained from the use of cathartics to warrant their use

As the infection clears a careful return to a normal diet is necessary It is wise to permit sugar and starches liberally Milk should be withheld until recovery is complete Activity should be limited for 3 or 4 days after an attack, since nausea or vomiting may return

Prophylaxis

Little is known about the exact method of transmission of this disease but it is probable that entry is made through both the respiratory and the gastro intestinal tracts Avoidance of contact with those ill with the disease care in food handling, and segregation of the acute cases are indicated

Phlebotomus Fever

The treatment of phlebotomus fever also known as pappataci fever, *sandfly fever* and *three day fever* is *entirely symptomatic* *Bed rest* with an adequately nourishing diet and sufficient fluids to maintain fluid balance as outlined in Part 1 should be carried out

There is no known specific drug therapy, the sulfonamides and penicillin are of no value unless a bacterial infection susceptible to these drugs is also present Aureomycin should be given a trial in an initial dose of 2 0 gm by mouth followed by 0 5 to 1 0 gm 4 times a day Acetylsalicylic acid 0 3 to 0 6 gm, or acetophenetidin 0 3 gm and codeine phosphate 0 03 gm, may be given as needed for the headache muscle and joint pains If the headache is worse at night morphine sulfate, 8 mg should be given hypodermically at bedtime If headache is intractable it may be relieved by a lumbar puncture Convalescence may be quite prolonged Death is very rare

or plasma preparation, if made from the blood of many contributors, is likely to be contaminated As yet there is no effective way of destroying the virus in these preparations Ultraviolet-light irradiation shows some promise of destroying virus in serum products, but it has not prevented the disease after the use of some pooled bloods Virus in human serum albumin is destroyed by heating the albumin solution to 60° C for 10 hours

Homologous plasma and serum products should be employed only when definitely necessary and with the knowledge that infection is a possibility Where it is necessary to use homologous plasma, the material should be secured from as few individuals as possible and all those who have had jaundice in the past or who have been in contact with patients with viral hepatitis should be excluded

Blood for transfusions should be secured from as few individuals as possible and individuals who give a history of jaundice should be excluded It is desirable to exclude individuals who have been in close contact with jaundiced patients since in this group there are likely to be carriers Persons with no history of jaundice may be carriers

All needles syringes and other instruments in contact with human blood must be washed thoroughly and sterilized carefully after each use

Gamma globulin 10 cc intramuscularly 1 and 2 months after plasma transfusion, may be of value

Yellow Fever

There is no specific treatment for yellow fever Isolation with protection from access of mosquities is imperative Bed rest, a very simple diet largely liquid and high in carbohydrate and protein, and constant nursing care are necessary Vomiting usually occurs and prevents adequate food and fluid intake therefore intravenous normal saline solution with 5 per cent glucose should be used freely given slowly, in order to make up any deficiency in fluid intake and prevent dehydration To this the daily addition of thiamine hydrochloride 10 mg ascorbic acid, 100 mg, and nicotinic acid 50 mg is recommended If hemorrhagic manifestations appear vitamin K 2 to 4 mg should be given daily Cracked ice and nupercaine lozenges (Nuporals) are recommended to relieve vomiting When vomiting ceases such foods as rice water, crumbled egg yolk, and chicken broth should be given with gradual

BIBLIOGRAPHY

General

1 HOYNE, A and BROWN R H Modern Treatment of Contagious Diseases *Med Clin No Amer*, Jan 1950 p 134

Infectious Mononucleosis

1 CRONK G A Aureomycin in Infections Mononucleosis A Control Study *Am J Med*, 1951 ccxii p 413

Herpes

1 EBERT M H The Herpes Problem *Med Clin No Amer*, Jan 1949 p 145

2 FINLAND M FINNERTY E F Jr COLLINS H S BAIRD J W GOCKE T M and KASS E H Aureomycin Treatment of Herpes Zoster *N E J Med* 1949 ccxli p 1037

3 KASS E H AYCOCK R R and FINLAND M Clinical Evaluation of Aureomycin and Chloramphenicol in Herpes Zoster *N E J Med* 1952 ccxlvi p 167

4 KILBOURNE E D and HORSFALL F L Jr Primary Herpes Simplex Virus Infection of the Adult *Arch Int Med*, 1951 lxxxviii, p 495

5 MARSH W C Treatment of Herpes Zoster with Protamide *U S Armed Forces Med Bull*, 1950 i p 1045

Viral Hepatitis

1 HAVENS W P Jr Infections Hepatitis' *Medicine*, 1948 xxvii p 279

2 MULTIPLE AUTHORS Symposium on Viral Hepatitis *Am J Med* 1950 viii p 559

3 POST J Studies on Sequelae of Acute Infectious Hepatitis *Ann Int Med* 1950 xxxiii p 1378

4 STOKES J Jr BLANCHARD M NEEFE J R GELLIS S S WADE, G R HAMPIL B and SPIZIZEN J Methods of Protection against Homologous Serum Hepatitis Studies on Protective Value of Gamma Globulin in Homologous Serum Hepatitis SH Virus *Jour Amer Med Assoc*, 1948 cxxxviii pp 336 341

5 WATSON C J The Prognosis and Treatment of Hepatic Insufficiency *Ann Int Med* 1949 xxxi p 405

6 WEINSTEIN L Virus Diseases Their Diagnosis and Management *Med Clin No Amer*, Sept 1950 p 1319

necessary to give amphetamine (Benzedrine) sulfate, 5 to 10 mg 3 times a day, to secure relief Vaccination with dengue virus modified by intracerebral passage in mice has proved successful as a preventive measure

Foot and Mouth Disease, Epidemic Stomatitis

Treatment is symptomatic, as there is no effective specific therapy If fever is present bed rest is advisable during its continuance The skin lesions should have a sterile protective dressing wet with benzylkonium (Zephiran) chloride 1 1000 For local irritation and pruritus, applications of phenolated calomine lotion N F zinc oxide ointment U S P, or local anesthetic ointments such as 1 per cent dibucaine (Nupercaine) or 5 per cent ethyl aminobenzoate (Benzocaine) in a water soluble base are helpful For the mouth lesions, a weak potassium permanganate mouthwash, 1 2000, is advised Rinsing the mouth with aureomycin solution, 1 1000 or aureomycin troches may prove helpful

As there are no reports of man to-man transmission, the important thing in prophylaxis is to keep unpasteurized milk or butter from possible sources of infection and to avoid contact with cloven footed animals that are infected Foot and mouth disease is highly contagious and of very great economic significance Any probable case in man should, for this reason, be reported at once to the state public health service

Acute Viral Gastro enteritis

No specific treatment is known for this acute gastro-intestinal malady The attack will be shortened by absolute bed rest and abstinence from food A limited water intake is also indicated since the more rest the gastro intestinal tract gets the less will be the nausea and vomiting experienced Since the attack is usually short lived, there is little danger of dehydration If fluid is indicated and desired, however, it should be given gradually in the form of a few sips of water weak tea, or fruit juices Occasionally fluids must be given by vein in the form of normal saline solution or 5 per cent glucose in normal saline The camphorated tincture of opium U S P (paregoric) in 8 cc doses after each stool is useful in control of the diarrhea as are preparations containing aluminum hydroxide and kaolin (Kaomagma) or aluminum hydroxide and pectin (Kaopectate) These are given in a dose of 16 cc 3 or 4 times a day

BIBLIOGRAPHY

General

1 HOYNE A and BROWN R H Modern Treatment of Contagious Diseases *Med Clin No Amer*, Jan 1950 p 134

Infectious Mononucleosis

1 CRONK G A Aureomycin in Infectious Mononucleosis A Control Study *Am J Med*, 1951 CCXII p 413

Herpes

1 EBERT M H The Herpes Problem *Med Clin No Amer*, Jan 1949 p 145
2 FINLAND M FINNERTY E F Jr COLLINS H S BAIRD J W GOCKE T M and KASS E H Aureomycin Treatment of Herpes Zoster *N E J Med* 1949 CCXLI p 1037
3 KASS E H AYCOCK R R and FINLAND M Clinical Evaluation of Aureomycin and Chloramphenicol in Herpes Zoster *N E J Med* 1952 CCXLVI p 167
4 KILBOURNE E D and HORSFALL F L Jr Primary Herpes Simplex Virus Infection of the Adult *Arch Int Med*, 1951 LXXXVIII p 495
5 MARSH W C Treatment of Herpes Zoster with Protamide *U S Armed Forces Med Bull* 1950 I p 1045

Viral Hepatitis

1 HAVENS W P Jr Infectious Hepatitis *Medicine*, 1948 XXVII, p 279
2 MULTIPLE AUTHORS Symposium on Viral Hepatitis *Am J Med* 1950 VIII p 559
3 POST J Studies on Sequelae of Acute Infectious Hepatitis *Ann Int Med* 1950 XXXIII p 1378
4 STOKES J Jr BLANCHARD M NEEFE J R GELLIS S S WADE G R HAMPIL B and SPIZIZEN J Methods of Protection against Homologous Serum Hepatitis Studies on Protective Value of Gamma Globulin in Homologous Serum Hepatitis SH Virus *Jour Amer Med Assoc* 1948 CXXXVIII pp 336 341
5 WATSON C J The Prognosis and Treatment of Hepatic Insufficiency *Ann Int Med* 1949 XXXI p 405
6 WEINSTEIN L Virus Diseases Their Diagnosis and Management *Med Clin No Amer* Sept 1950 p 1319

Prophylaxis

The chief vector of this disease is the sandfly, *Phlebotomus papatasii*, against which precautions should be taken Since it can penetrate the ordinary mosquito netting a finer mesh netting should be used for screening Insecticides such as chlorophenothane (DDT) are extremely useful

PSITTACOSIS ORNITHOSIS

Treatment in general should be symptomatic as described in Part I As the disease in man usually includes a pneumonic process treatment should include symptomatic treatment for symptoms from that source as described in the section on Non bacterial or Viral Pneumonia Aureomycin should be given in an initial dose of 2 0 gm by mouth, followed by 0 5 to 1 0 gm 4 times a day Chloramphenicol and terramycin in similar dosage are also effective If thrombophlebitis occurs, bishydroxycoumarin (Dicumarol) therapy as described in the treatment of coronary artery thrombosis should be given Venous ligation should be considered in cases with serious or widespread venous involvement

Penicillin is of value against some strains, but the wider spectrum antibiotics—aureomycin, chloramphenicol, and terramycin — are more effective

Prophylaxis consists of the recognition of the presence of psittacosis in birds of the parrot family including, among others parrots, parakeets and lovebirds, and in canaries and finches, with their prompt extermination It is safer to kill promptly any sick pet birds of this group than to await certainty that they have psittacosis A long quarantine of any of them before taking them into the home as pets is a necessary precaution Avoidance of intimate contact with birds, their droppings, and the dust from cages and roosts is also wise A patient with psittacosis should be kept in isolation with particular care that contact with his sputum and with the expired droplet moisture incident to his coughing, sneezing and/or deep breathing is avoided To this end, masks should be used by all in attendance, and other usual techniques of isolation should be observed, sputum and materials in contact with mouth and nose should be promptly destroyed Active immunization can be given with chick embryo vaccine

PART V

RICKETTSIAL AND BARTONELLIAL INFECTIOUS DISEASES

CHAPTER XV

RICKETTSIAL GROUP OF DISEASES

Typhus

Treatment of typhus consists of (1) antibiotic therapy and (2) general measures and symptomatic therapy If the former is promptly effective the latter directions become correspondingly less important, and their use can be reduced in time and extent of application to such as are usually advised for infectious diseases of relatively short duration and very moderate severity

Antibiotic Therapy

Aureomycin chloramphenicol and terramycin are effective So far there has not been enough comparable use of these to determine which should have preference nor is it known whether in case of failure of one the other would be effective If in a given patient one causes toxicity shift to the other is advised

Aureomycin should be given orally so that the patient receives on the first day 6 gm in divided doses given at 3 hour intervals and then 4 gm daily in divided doses until the temperature is reduced to normal It is then continued at 2 gm doses daily for 5 more days

Chloramphenicol although highly effective should be reserved for

Prophylaxis

The chief vector of this disease is the sandfly, *Phlebotomus papatasii*, against which precautions should be taken Since it can penetrate the ordinary mosquito netting, a finer mesh netting should be used for screening Insecticides such as chlorophenothane (DDT) are extremely useful

Psittacosis Ornithosis

Treatment in general should be symptomatic as described in Part I As the disease in man usually includes a pneumonic process, treatment should include symptomatic treatment for symptoms from that source as described in the section on Non bacterial or Viral Pneumonia Aureomycin should be given in an initial dose of 2 0 gm by mouth, followed by 0 5 to 1 0 gm 4 times a day Chloramphenicol and terramycin in similar dosage are also effective If thrombophlebitis occurs, bishydroxycoumarin (Dicumarol) therapy as described in the treatment of coronary artery thrombosis should be given Venous ligation should be considered in cases with serious or widespread venous involvement

Penicillin is of value against some strains but the wider spectrum antibiotics—aureomycin, chloramphenicol, and terramycin — are more effective

Prophylaxis consists of the recognition of the presence of psittacosis in birds of the parrot family including, among others parrots, parakeets, and lovebirds, and in canaries and finches, with their prompt extermination It is safer to kill promptly any sick pet birds of this group than to await certainty that they have psittacosis A long quarantine of any of them before taking them into the home as pets is a necessary precaution Avoidance of intimate contact with birds, their droppings, and the dust from cages and roosts is also wise A patient with psittacosis should be kept in isolation, with particular care that contact with his sputum and with the expired droplet moisture incident to his coughing, sneezing and/or deep breathing is avoided To this end masks should be used by all in attendance, and other usual techniques of isolation should be observed, sputum and materials in contact with mouth and nose should be promptly destroyed Active immunization can be given with chick embryo vaccine

transfusions and other measures as described under Typhoid Fever Phenylephrine (Neosynephrine) hydrochloride 5 mg intramuscularly or 10 to 15 mg orally or hydroxyamphetamine (Paredrine) hydrobromide 10 mg intramuscularly or 20 to 40 mg orally, may be of help in combatting circulatory failure especially if the blood pressure is low Oxygen is valuable in the presence of cyanosis and respiratory distress and is given by mask as described under Pneumonia An oxygen concentration of approximately 80 to 90 per cent is preferable to nearly pure oxygen Care must be taken to avoid irritation and the anti expectorant effects of oxygen Drugs of the digitalis group should not be used except for patients with congestive failure of a coincidental chronic heart disease

Analgesics such as acetylsalicylic acid 0 3 to 0 6 gm by mouth methadone, 5 mg meperidine (Demerol) hydrochloride, 50 to 100 mg intramuscularly or orally, or morphine sulfate 8 mg hypodermically will prove helpful for headaches, restlessness insomnia, and muscular aches and pains Sedation for restlessness, irritability and insomnia may prove valuable Phenobarbital 15 to 30 mg given 3 or 4 times in 24 hours will usually suffice

Prophylaxis

The patient and attendants should be protected from lice and rat fleas Chlorophenothane (DDT) should be used freely as a dusting powder or spraying mixture on everything in any way in contact with a patient developing typhus and throughout his surroundings Rats and mice should be exterminated as far as possible and their burrows and surroundings treated with DDT remember that fleas speedily leave the dead animals

The patient s attendants and all individuals likely to come in contact with typhus infected lice or fleas should receive subcutaneously 1 cc of the Cox type of anti typhus vaccine repeated in 10 to 14 days with a booster dose every 6 months as long as the individual is likely to come in contact with patients having typhus fever or with potential vectors of the disease In the presence of an epidemic a booster dose should be given The peal period of immunity is reached approximately 3 months after the inoculation The only contraindication to the use of the vaccine is egg allergy

Individuals in infested areas should wear protective clothing consisting of high boots garments fitting snugly at the wrist and neck gloves, and head protection. Dusting daily with 10 per cent DDT powder affords further protection Careful daily inspection of the entire body for the presence of ticks is essential Special attention should be given to the scalp, axillae pubic region behind the ears and between the toes

Ticks should be removed carefully with forceps after touching them with a drop of kerosene or holding a lighted cigarette near by in order to force them to withdraw the mouth parts The bite area should be touched with an antiseptic They should never be handled with the bare hands, as infection may take place in this manner

Immunization with a vaccine made from killed ground up ticks or egg cultivated rickettsia is of definite value and is recommended for all who reside in or plan to visit areas known to have infected ticks The vaccine is given in 2 injections of 2 0 cc each at an interval of 5 days Booster doses should be given at the beginning of each season

Bullis Fever

As with other rickettsial infections the treatment of bullis fever is based on the prompt administration of aureomycin chloramphenicol or terramycin These should be given promptly as described for Rocky Mountain Spotted Fever and Typhus Para aminobenzoic acid has been replaced by these more active drugs Patients should receive symptomatic treatment as outlined in Part 1 Adequate fluid balance should be maintained The severe headaches and generalized aching should be controlled with analgesics Acetylsalicylic acid 0 3 to 0 6 gm or acetphenetidin 0 2 gm by mouth, or codeine phosphate, 30 mg hypodermically should be given Occasionally in severely painful cases morphine sulfate 8 mg hypodermically is indicated

Anemia when present should be treated with ferrous sulfate or ferrous gluconate 1 to 2 gm daily Patients with severe anemia may require whole blood transfusions

Scrub Typhus Tsutsugamushi Fever

Scrub typhus should be treated as has been described for Typhus

cases that do not respond to aureomycin or terramycin It should be given orally in an initial dose of 60 mg per kilogram of body weight, followed by 250 mg every 2 hours until the temperature becomes normal This dose is then continued at 3- or 4 hour intervals thereafter for 5 more days

Terramycin given in the same dosage and manner as described for chloramphenicol is also effective

A hyper-immune rabbit serum is helpful, and when the infection is refractory to antibiotics, or in exceedingly serious cases, it should be given in the dosage directed by the manufacturer

Penicillin should certainly be given if a complicating infection sensitive to it develops

If the measures above are not effective para aminobenzoic acid should be given by mouth in an initial dose of 4 to 8 gm followed every 2 hours by 1 to 3 gm so long as there is fever These rapidly repeated doses are needed to maintain an adequate blood level on account of the very rapid excretion of the drug

General Measures and Symptomatic Therapy

General measures of treatment as described in Part 1 and under Typhoid Fever should be applied at once to patients with typhus Bed rest is imperative accompanied by competent nursing care Ample fluid intake not less than 3000 cc every 24 hours, is very important, if liquid is not being taken by mouth, the deficiency should be made up parenterally with 5 per cent glucose in normal salt solution Diet should be simple but of high calorie value if possible as in typhoid, it should contain 5 to 10 gm of sodium chloride every 24 hours Bed sores are very likely to occur, they should be prevented as far as possible, by thorough cleaning, drying and powdering of the skin on the back and especially over the buttocks, by relieving pressure with rings or doughnuts where it is likely to be marked and by frequent shifts of the patient's position At the first sign of a developing bed sore cleanliness, dryness, and prevention of continued pressure are imperative If oliguria becomes marked, increased fluid should be given parenterally but very slowly Headache vomiting and hiccough are often relieved by lumbar puncture with slow moderate reduction of the elevated intraspinal pressure Circulatory insufficiency should be treated by plasma or blood

be adequate prophylaxis for infection from this source Cases have also appeared in workers handling wool and animal hair in dusty atmospheres Patient to patient transfer also occurs, consequently, isolation as for typhoid fever is indicated

Rickettsialpox

This mild disease caused by *R akari* usually responds well to symptomatic measures as described in Part 1 Antibiotic therapy with aureomycin and possibly chloramphenicol or terramycin is helpful

Pretibial Fever Bushy Creek Fever

This is an infectious disease of probable virus etiology in which patients are only mildly sick Simple symptomatic treatment usually suffices for it Aureomycin may prove helpful in more severe cases No fatalities or residual effects have been observed

Colorado Tick Fever

Treatment is entirely symptomatic for this disease The course is benign Aureomycin is indicated if prompt recovery does not occur

Prophylaxis consists in avoidance of contact with *D Andersoni* by the measures recommended for Rocky Mountain Spotted Fever A virus vaccine has been developed experimentally which gives successful active immunization

Coxsackie Disease, including Herpangina

There are no specific measures available for the treatment of this recently recognized virus infection Fortunately the usual symptomatic treatment is satisfactory For the pleurodynia which may develop the measures recommended for acute pleurisy should be carried out

Prophylaxis consists in the avoidance of contact with patients having the disease The virus is found in the respiratory and gastro intestinal tracts consequently respiratory precautions are necessary and the stool should be disinfected

Rocky Mountain Spotted Fever

This rickettsial disease, now known to be much more widespread than formerly believed, responds readily to aureomycin, chloramphenicol, and terramycin Para-aminobenzoic acid and rabbit anti serum used extensively until recently, have been replaced by these more effective antibiotics Prompt bed rest and good nursing care are essential Special attention should be given to the skin over pressure areas in order to avoid formation of decubital ulcers, and the patient should be shifted frequently enough to avoid hypostatic pneumonia The rapid response to the newer antibiotics has, in most cases, so shortened the course of the disease that there is much less possibility of liver injury, and consequently dietary factors are of less significance If, however, the infection is severe or prolonged, there is usually considerable liver damage, and in these cases the diet should be high in protein (2 or 3 gm protein per kilogram of body weight), high in carbohydrate low in fat, and abundantly supplemented with vitamins especially those of the B complex

Sufficient physiological salt solution or 10 per cent glucose solution should be given to correct any dehydration Plasma or whole blood transfusions should be given when needed to prevent or treat shock If cardiac decompensation is present or develops, the patient should be digitalized

Aureomycin and terramycin are highly effective and quickly control the infection when they are given in an initial oral dose of 2 0 gm followed by 0 5 to 1 0 gm every 3 or 4 hours Chloramphenicol is also highly effective and should be given if aureomycin or terramycin is ineffective It is given in similar dosage With this regime the temperature usually falls to normal within 3 days and clinical improvement is apparent within 24 to 48 hours

Prophylaxis

The disease is carried and spread by ticks Man becomes infected when bitten by the infected tick or by handling them with unprotected hands Heavily infested areas may be cleared of ticks by dusting them with 2 to 3 pounds of pure chlorophenothane (DDT) per acre Dogs, cats and other domestic animals carry the ticks and contaminate their surroundings Dusting them and rugs sofas chairs, and other sites with which they are likely to come in contact with 10 per cent DDT at least once weekly will prevent infestation

CHAPTER XVI

DISEASES CAUSED BY BARTONELLAE

Oroya Fever and Verruga Peruana

Streptomycin in the usual dosage is the treatment of choice in this serious disease The usual general measures outlined in Part 1 are indicated Penicillin in full dosage may be of some value Vaccination with formalized suspensions of *Bartonella bacilliformis* is apparently of value and ameliorates the course of serious cases Immune serum may be given although apparently it is not very effective Liver extract and iron should be given to combat the anemia Transfusions are helpful in the severely anemic cases

Prophylaxis

Protection from the sandfly *Phlebotomus verrucarum* or *P noguchii*, and also possibly from ticks should be carried out Tick proof clothing should be worn in infested areas Liberal use of Chlorophenothane (DDT) powder on both animals and individuals is recommended and liberal dusting of infected areas with 2 to 3 pounds of DDT per acre will destroy the vectors Avoidance of the infested area during the hours of darkness and the use of fine mesh nets, screens and sandfly proofed buildings are advised

BIBLIOGRAPHY

1 ALDANA L GASTELUMENDI R and DIEGUEZ J Streptomycin in Carrions Disease *Arch Peruanos de Pat y Clin Lima* 1948 II p 171

Prophylaxis

Avoidance of the mite vector of the *Trombicula* genus is of primary importance in prophylaxis, since no prophylactic vaccine is available at present Impregnation of clothing with such chemicals as dimethyl phthalate dibutyl phthalate or benzyl benzoate seems to have been effective against these mites

Trench Fever

This rickettsial infection usually of short duration, is best treated by bed rest high-protein high calorie diet and fluids as indicated Muscle pains and generalized aches, so common in the disease, are best controlled with methadone 5 to 10 mg meperidine (Demerol) hydrochloride, 50 to 100 mg or acetylsalicylic acid, 0 6 gm, at 3- to 4 hour intervals Nausea and anorexia may be relieved by antacids, such as aluminum hydroxide gel or a mixture of aluminum hydroxide and magnesium trisilicate (Gelusil) Aureomycin chloramphenicol, or terramycin given as outlined under Typhus is advised

Q (Queensland) Fever

The Australian and American forms of Q fever are caused by *C burneti* and their treatment is the same As the patients are usually only mildly ill, bed rest, a nourishing diet and adequate fluids may be all that are required Aureomycin is advised in a dose of 4 0 gm daily, in equally divided doses every 3 hours for 4 days and then in doses of 2 0 gm a day divided similarly for 4 days Terramycin should be given in similar manner and dosage if aureomycin is not effective in an individual patient

In humans pneumonitis forms an important part of the disease, clinically this usually resembles other atypical (viral) pneumonias Complete recovery with symptomatic treatment is the rule It seems worth while however, to give antibiotic therapy to these patients even though results are not as gratifying as are those obtained from the use of these agents in other rickettsial infections

There is recent evidence that cattle and milk may be sources of the infection in this country Proper pasteurization of milk is thought to

CHAPTER XVI

DISEASES CAUSED BY BARTONELLAE

Oroya Fever and Verruga Peruana

Streptomycin in the usual dosage is the treatment of choice in this serious disease The usual general measures outlined in Part 1 are indicated Penicillin in full dosage may be of some value Vaccination with formalized suspensions of *Bartonella bacilliformis* is apparently of value and ameliorates the course of serious cases Immune serum may be given although apparently it is not very effective Liver extract and iron should be given to combat the anemia Transfusions are helpful in the severely anemic cases

Prophylaxis

Protection from the sandfly *Phlebotomus verrucarum* or *P noguchii*, and also possibly from ticks should be carried out Tick proof clothing should be worn in infested areas Liberal use of Chlorophenothane (DDT) powder on both animals and individuals is recommended and liberal dusting of infected areas with 2 to 3 pounds of DDT per acre will destroy the vectors Avoidance of the infested area during the hours of darkness and the use of fine mesh nets, screens and sandfly proofed buildings are advised

BIBLIOGRAPHY

1 ALDANA L GASTELUMENDI R and DIEGUEZ J Streptomycin in Carrions Disease *Arch Peruanos de Pat y Clin Lima,* 1948 II p 171

BIBLIOGRAPHY

Rickettsial Group of Diseases

1 HARRELL G T Jr Rocky Mountain Spotted Fever," *Medicine*, 1949 xxviii, p 333
2 KILLOUGH J H and MAGILL G B Terramycin in Epidemic Typhus, Amebic Dysentery and Typhoid,' *Jour Amer Med Assoc*, 1951, cxlvii, p 1737
3 LEY H L Jr WOODWARD T E and SMADEL, J E, Chloramphenicol in Treatment of Typhus ' *Jour Amer Med Assoc*, 1950, cxliii p 217
4 PARROTT R H ROSS S BURKE, F G and RICE, E. C Herpangina Clinical Studies of a Specific Infectious Disease, *N E J Med*, 1951 ccxlv p 275
5 ROSE, H KNEELAND Y and GIBSON C "Treatment of Rickettsialpox with Aureomycin *Am J Med*, 1950 ix p 300
6 WOODWARD T E Chloromycetin and Aureomycin, Therapeutic Results ' *Ann Int Med*, 1949 xxxi, p 53

PART VI

PROTOZOAN INFECTIONS

CHAPTER XVII

DISEASES CAUSED BY TREPONEMATA

Syphilis

At the present time (1952) penicillin is regarded as the most effective agent that we have for the treatment of syphilis and the one, all in all, that is simplest to use. Its use is advised for the treatment of many clinical varieties of syphilis with repetition if apparent cure does not result from the first course of treatment, or if relapse occurs. Consequently the use of penicillin in the treatment of syphilis will be described first. In later pages other antibiotics, arsenobismuth and tryparsamide therapy will be described. In certain circumstances metal therapy is still advised, either singly or in various combinations with penicillin. Following this, other therapeutic procedures such as malarial pyretotherapy, will be described and their uses discussed.

It must be acknowledged that to date no way of treating syphilis can be considered to be completely satisfactory. With all methods so far used, there has been a considerable percentage both of early failures to cure and of the appearance after treatment of late serious manifestations. The percentage of the former has been reduced, especially since the use of intensive penicillin therapy has been in vogue. What the effect of that will be on the late appearance of serious manifestations of syphilis can only be surmised now, since these manifestations, even without any treatment, may be delayed for 25 or even more years.

Before any form of treatment, every patient should have a thorough physical examination with record of the presence and appearance of any lesions possibly syphilitic, a serum test for syphilis, preferably a quantitatively titrated test, and a spinal puncture with cytological, serological, and chemical study of the spinal fluid.

without hospitalization by the use of slowly absorbed preparations—if the patient will return for treatment as often as directed if directions for protection of others against syphilitic infection are followed rigorously, and if all directions given by the physician are followed Obviously there will be greater certainty of all of this when the patient is under continuous hospitalization A desirable compromise between the two can be worked out on the basis of hospitalization during the period of greatest infectivity followed by an ambulatory regime This program will prove in the long run both practical and satisfactorily effective and usually the regime of choice

Of the various penicillin preparations now available pure crystalline penicillin G or procaine penicillin G with 2 per cent aluminum monostearate is the preparation of choice Penicillin can be used in aqueous solution intravenously or intramuscularly at short intervals, 3 or 4 hours the intramuscular route usually being preferred Penicillin is also combined with procaine in sesame oil and 2 per cent aluminum monostearate or with procaine in aqueous suspension with 2 per cent aluminum monostearate These are to be given intramuscularly not more often than once every 24 hours the last mentioned produces less persisting local pain and less possibility of sensitivity reactions than the preparations containing oil These preparations for intramuscular use are usually marketed in concentrations of 300,000 Oxford units of penicillin per cc of suspension

Acquired, Early, Syphilis The basal penicillin treatment described below is to be used in treating adults with seronegative or seropositive primary secondary, and early latent syphilis Accumulated evidence indicates that the minimal effective dosage of penicillin for the treatment of primary and secondary syphilis is approximately 2,400 000 units For infants and very young children doses smaller than those given in the basal treatment should be used

Basal penicillin treatment as indicated in the preceding paragraph should consist of 50 000 units of penicillin in aqueous solution, given intravenously or intramuscularly every 3 hours 8 times daily for 8 to 10 days (total dose 3 200 000 units) or tri weekly intramuscular injections of 600 000 units (2 cc) of procaine penicillin in oil with 2 per cent aluminum monostearate for 3 weeks (total dose 3 600 000 units) If procaine penicillin in aqueous suspension is to be used 600 000 units (2 cc) should be given intramuscularly every 24 hours for 8 injections (total dose 4 800 000 units)

Penicillin Treatment

Two considerations or desiderata are of prime importance in the treatment of syphilis (1) to make the patient infected with the *Treponema pallidum* speedily non infective to others so as to check the dissemination of syphilis, (2) to prevent the development of serious, late manifestations of syphilis particularly symptomatic neurosyphilis and cardiovascular syphilis Experience to date with penicillin treatment of syphilis seems to show that a large proportion of patients can be rendered quickly non infective by the regime of time-dosage of penicillin soon to be described a proportion which can be much increased if treatment of all cases is begun very soon after infection, and if those failing to become non-infective after the first course of treatment are quickly re treated It is too early to say that late serious manifestations of syphilis can be entirely prevented by such regimes of penicillin therapy These late manifestations of syphilis may not, and usually do not, develop for 10 to 30 years after the first infection, and that they will not develop cannot be stated with definiteness until many patients treated with penicillin have been observed over these long years However, the probability that penicillin therapy will prevent most of them is attested by penicillin rendering very many patients clinically and serologically negative some of whom have demonstrated that they are susceptible again to reinfection with syphilis Under these circumstances it seems justifiable to recommend penicillin alone for the treatment of all patients with syphilis unless the use of penicillin is for some reason not practicable There are a few exceptions to this as will be discussed later, where penicillin should be combined with pyretotherapy or with tryparsamide

The use of penicillin in the treatment of syphilis is much simpler than was the former treatment with the metals arsenic and bismuth, because of the very low toxicity of penicillin its ease of preparation, the relative simplicity of giving it the much shorter time required for the attainment of satisfactory therapeutic results and the great reduction in the number of patients failing to complete treatment in comparison with this factor in previously used regimes of therapy For these reasons it seems now to be with few exceptions the preferred form of treatment

In the use of penicillin it is preferable to hospitalize the syphilitic patient, this is especially important during the infective stages of the disease When this is not possible, the patient can be treated effectively

any neurological symptoms accompanied by a study of the spinal fluid, even if therapeutic response has been satisfactory

The plan of penicillin treatment with its indicated dosages as just described should be applied to patients with early infectious acquired syphilis with or without complications including early neurosyphilis It should also be applied to patients with late acquired syphilis osseous and visceral including cardiovascular syphilis and all forms of neuro syphilis except Erb s spastic paraplegia, general paresis taboparesis tabes dorsalis and primary optic atrophy, in which pyretotherapy should be an added therapeutic procedure. With nerve deafness due to syphilis, probably induced fever should also be used with the penicillin therapy

Acquired Latent Syphilis For patients with late latent syphilis i e seropositive cases without signs or symptoms and no evidence of cardiovascular or neurosyphilis and with normal spinal fluid penicillin should be given as recommended for acquired early syphilis These cases are very important because they have undergone generalized dis semination of treponemata and are the cases that may develop symptomatic late syphilis Consequently effort should be made to render them seronegative by using penicillin or that failing by giving them a course of arsenobismuth treatment and they should be re examined as recom mended for active syphilis so that they may be re treated at once if evidences of late symptomatic syphilis appear

If the various types of syphilis — early late and latent — are treated as already advised the number subsequently developing cardiovascular or symptomatic neurosyphilis will undoubtedly be reduced Thorough treatment of early syphilis with repeated follow up examinations and indicated re treatments is actually the best form of treatment for these late manifestations it is prophylactic therapy and these forms of syphilis are easier to prevent than to cure

For *asymptomatic* neurosyphilis cardiovascular benign late and visceral syphilis the following minimum dosage schedules are recommended on the basis of presently available information with crystalline pen icillin in aqueous solution, 100 000 units intramuscularly every 3 hours 8 times daily for 12 days (total dose 9 600 000 units) procaine pen icillin G in aqueous suspension 900 000 units (3 cc) intramuscularly every 24 hours for 12 injections (total dose 10 800 000 units) procaine penicillin G in oil with 2 per cent aluminum monostearate 900 000 units (3 cc) intramuscularly every 48 to 72 hours for 12 injections (total dose 10 800 000 units)

Cardiovascular Syphilis If cardiovascular symptoms do appear full

If, after such treatment the patient's serum is not negative to an accepted form of serological test for syphilis, or if a positive serum reaction develops, or if the spinal fluid previously serologically or cytologically positive, has not become negative, or if any syphilitic lesions remain or return, then the course of treatment with penicillin should be repeated

For success in the treatment of syphilis, it is imperative that patients be kept under observation over a period of many years The following plan for this is suggested for the first year, a monthly examination with thorough search for lesions of skin and/or mucous membranes and a quantitatively titered serological test for syphilis for the second year, the same studies every 3 months, for the third and for subsequent years these examinations should be made preferably every 6 months and at least once a year If the spinal fluid was negative before treatment, it should be rechecked in the second year, provided the blood serologic test remains low or has become negative, if blood tests are positive or increase in titer rechecking of the spinal fluid should be made more frequently If before treatment the spinal fluid was positive, rechecking should be at intervals of 3 to 6 months until it has become normal and remained so for several years If at any of these re examinations syphilitic lesions are found or if seronegativity has disappeared, or if the spinal fluid becomes seropositive or develops an increased cell count, re treatment should be begun If the spinal fluid has become abnormal, immediate re treatment is imperative, unless some other cause for the spinal fluid abnormality, i e a non syphilitic one can be proved To succeed in the treatment of syphilis in the sense that the patient finally be completely cured, such re examination over many years are necessary with treatments repeated whenever any reactivity of syphilitic infection is detected A return to frequent re-examinations should be taken up again after such repeat treatments have been carried out Finally, if evidences of activity of the syphilitic process fail to disappear after re-treatments with penicillin, arsenobismuth treatments should be commenced

There will be patients in whom seronegativity fails to be produced by repeated penicillin treatments while all other evidences of syphilis have disappeared For these patients further courses of penicillin treatment seem indicated only when the serum reaction shows a quantitatively increasing titer or syphilitic lesions appear If these patients fail to respond satisfactory to penicillin then a shift to arsenobismuth therapy should be made All of these patients should be re examined often with especial search for the presence of any signs of cardiac involvement or of

ative changes predominate Active cases respond promptly inactive slowly to treatment since with activity treponemata are numerous in the lesions with inactivity very scarce and it is the treponemata which are most effected by treatment

Patients with active neurosyphilis in the sense just stated should be given penicillin as already described under Acquired Early Syphilis except that the total dose should be increased to 10 000 000 units or more In general crystalline penicillin G in aqueous solution appears to be the drug of choice and should be given in doses of 100 000 units at 3 hour intervals over a period of 12 to 20 days for a total of 9 600 000 to 15 000 000 units Patients with inactive neurosyphilis in this same sense i e with predominately degenerative lesions should receive simultaneously penicillin and pyretotherapy as described later under appropriate headings These are the patients grouped clinically as having Erb s spastic paraplegia tabes dorsalis paresis taboparesis syphilitic optic atrophy and possibly syphilitic nerve deafness

In *late cutaneous* mucous membrane and osseous syphilis penicillin in a total dosage of 6 000 000 units has proved to be quite effective This may be given as aqueous procaine penicillin 600 000 units (2 cc) daily for 10 days or as procaine penicillin in oil with 2 per cent aluminum monostearate 600 000 units twice a week for 5 weeks

Congenital Syphilis Penicillin is the treatment of choice for congenital syphilis of all forms except under certain conditions described in the following paragraphs

Infantile Congenital Syphilis For this either the aqueous penicillin solution given intravenously or intramuscularly or the more slowly absorbed preparations given *intramuscularly may be used If the aqueous* solution is used 400 000 units of penicillin per kilogram of body weight divided into 80 to 120 aliquot doses given intravenously or intramuscularly at 3 hours intervals is recommended Instead of this the same number of units of penicillin (400 000) in the form of penicillin procaine in oil with aluminum monostearate may be divided into 6 aliquot doses each given at 2 or 3 day intervals In general the more slowly absorbed penicillin preparations just described are to be preferred except for extremely ill patients for which the aqueous solution at 2 to 3 hour intervals is probably better Such lesions as condylomas cutaneous erosions and snuffles clear rapidly often in 24 hours under this treatment osteochondritis and osteoperiostitis more slowly bone pain and pseudoparalyses vanish promptly while radiographic bone

penicillin treatment as already described for acquired early syphilis should be begun at once unless there are clinical evidences of cardiac decompensation It has seemed safe to give penicillin in full dosage immediately to patients with cardiovascular syphilis after cardiac decompensation, if present has been controlled, i e without the preliminary treatment that was thought necessary with arsenical treatments Jarisch Herxheimer reactions have not been frequent and very few have been severe It is safer however to have these patients in the hospital during the early period of penicillin treatment so that, in case reactions appear, they may receive promptly any needed treatment It must be recognized that, if marked scarring has occurred in cardiovascular syphilis before treatment, penicillin treatment cannot be expected to change this to any great extent Still penicillin may bring improvement, and so each case of cardiovascular syphilis should undergo penicillin therapy

Neurosyphilis It is important to remember that neurosyphilis associated with early acquired syphilis is very often asymptomatic and that this is the stage at which treatment is particularly effective Consequently every syphilitic patient should have a spinal fluid study before treatment and another after completion of a course of treatment to check whether he has been made negative i e normal, if not normal, re treatment should be undertaken at once and this repeated until normality of spinal fluid is attained if that is possible and almost always it is possible This is in contrast to patients who have evidences of neurosyphilis one or two years after the primary infection, these patients are much more difficult to clear of their neurosyphilitic lesions

If the spinal fluid of syphilitics shows elevated cell count increased total protein, positive complement fixation, and/or positive colloidal gold or mastic test, under treatment cell count as a rule falls to normal first followed shortly by fall to normal of total protein content, usually within - to 6 months after treatment with penicillin has been started Colloidal tests next return to normal while the serology reaction may decrease much more slowly toward normal titer In some patients it may remain elevated even though decreased these are seroresistant cases and need prolonged and careful follow-up checks so that therapy may be resumed, if and when the serology reaction is found to have increased in titer

In neurosyphilis patients can be thought of as having both inflammatory and degenerative changes in the central nervous system and to be active or inactive in accordance with whether inflammatory or degener-

Aureomycin Chloramphenicol, and Terramycin

These wide spectrum antibiotics are also effective against *Treponema pallidum* They bring about rapid healing of primary and secondary lesions and a reversal of serology In a small number of patients followed for a short time there has been an excellent response to these agents Preliminary indications point to their being somewhat less effective than penicillin but this may be more a matter of total dosage than of less efficiency of these agents Further trial is necessary before the most suitable dosage can be determined Preliminary observations indicate that an initial dose of 2 0 gm followed by 1 0 gm every 4 hours until a total of approximately 75 gm has been given is effective

The ultimate role of these agents in the treatment of syphilis will have to wait until more patients have been observed

Arsenobismuth Treatment of Syphilis

If for any reason antibiotic therapy does not seem advisable for certain patients with syphilis or if it has not proved satisfactorily efficient then arsenic and bismuth can be used for those forms of syphilis for which penicillin treatment has already been described Various of the arsenicals such as arsphenamine, neoarsphenamine mapharsen et cetera may be used Of these mapharsen (oxophenarsine hydrochloride) because of the simplicity and ease of its preparation and its relatively slight toxicity is advised as the arsenical of choice mapharsen is to be given intravenously In addition to the arsenical bismuth is to be given Bismuth subsalicylate is a very satisfactory form of bismuth and is to be given intramuscularly deeply injected into the buttocks preferably in the outer upper quadrant with care to avoid the sciatic nerve make sure that the needle has not entered a vein by withdrawing the piston of the attached syringe to see if blood appears

Various schedules of dosage have been advised of which the following has proved quite satisfactory In the first course of treatment give 8 daily intravenous injections of 40 mg of mapharsen and an intramuscular injection of 0 2 gm of bismuth subsalicylate on the first third fifth seventh and ninth days, making the total of mapharsen 320 mg and *of bismuth subsalicylate 1 0 gm* Thereafter weekly injections are to be given over a period of 18 months on some such schedule as the following mapharsen for 8 weeks bismuth for 4 weeks expressed as 8 ars –4 bi and thereafter 6 ars –6 bi 6 ars –6 bi, 6 ars –8 bi 6 ars –10

changes lag in clearing for some weeks or months If treatment is instituted in the first year of life however, normal, adult skeletal development can be expected Hepatomegaly, splenomegaly, and lymph node hyperplasias regress gradually following penicillin treatment The abnormal spinal fluid changes associated with early congenital syphilis usually become normal 6 to 12 months after penicillin therapy, the serology reaction being the last to change to normal

A Jarisch Herxheimer reaction occurs in about half of these early congenital cases after treatment with penicillin, but the reaction is usually characterized by fever alone

Late Congenital Syphilis If the syphilitic lesion is of more than 2 years duration results of treatment are apt to be less striking Interstitial keratitis and iritis particularly resist penicillin treatment Bilateral hydrarthroses (Clutton s joints) respond very little, if at all, to penicillin, even when combined with thermal therapy For these, if there is no response to penicillin and thermal therapy arsenobismuth may be used Recent evidence indicates excellent results in interstitial keratitis with 1 0 to 2 5 per cent cortisone acetate instilled into the conjuctival sac Neurosyphilis including vascular or meningovascular lesions and juvenile paresis taboparesis and tabes dorsalis is not infrequent in infants, although often not recognized in its early stages, this makes treatment much less effective than if given early in the development of the disease Most of the children with paresis taboparesis and tabes dorsalis will be in their teens and should receive the same dosage of penicillin as described for adults along with thermal therapy

Prevention of Congenital Syphilis Syphilis in the infant can be prevented if the mother is treated with penicillin during pregnancy—the earlier the better Even if penicillin therapy is begun late, good results can be expected if the course of treatment has been completed before the ninth lunar month of pregnancy Both the mother and the fetus will have a very large percentage of their syphilitic infections cured Treatment of the mother should be that described for the various forms of syphilis as they occur in non pregnant women with repeat examinations at monthly intervals and re treatment if any evidences of relapse or re infection are found Re treatment in succeeding pregnancies is not necessary if the treatment in the first pregnancy has been satisfactory as judged by the usual criteria already described for non pregnant patients

Penicillin administration to the mother does not cause increased uterine irritability and miscarriage

Pyretotherapy in Syphilis

For this the malarial form appears to be generally preferred to other forms, such as typhoid vaccine fever or the Kettering hypertherm method

Malarial Therapy Tertian *Plasmodium vivax*, malaria is recommended for malarial therapy Inject 2 to 5 cc of the donor s blood immediately into the recipient by either the intradermal subcutaneous, or intravenous route many prefer the intravenous route Cross matching of donor and recipient for agglutination is not needed If immediate injection is not possible the blood of the donor containing malarial parasites should be citrated (1 cc of 2 5 per cent sodium citrate solution to 10 cc of blood) at once and injected later The incubation period varies from a few to 20 days If it is more prolonged many advise repeat inoculation with 10 cc of malaria infested blood If fever does not begin in 10 days some advise using typhoid vaccine intravenously to institute mild fever which will often precipitate the desired malarial paroxysm At present 8 malarial paroxysms are regarded as a desired course of therapy During malarial pyretotherapy the patient should have the same sort of observation nursing care and general measure of treatment as described for naturally acquired malaria At the end of the therapy the malarial bout is to be terminated by the antimalarial drugs in dosage advised for the treatment of tertian malaria Usually with such therapeutic malaria repeat paroxysms after antimalarial drugs have been given are rare in sharp contrast to the usual course of recurrence in vivax malaria of natural mosquito origin Apparently there is little danger of malarial infection of others by mosquitoes biting patients undergoing malarial hyperthermia and then biting others

If fever in paroxysms goes beyond a maximum of 105 F it is well to stop promptly the malarial infection therapeutically and the same applies if it is evident that the malarial paroxysms are causing too great debility too much fall in blood pressure or if there are other evidences that the patient is doing badly Circulatory and other complications must be carefully watched for and if they occur the malarial paroxysms must be terminated To be most effective any form of pyretotherapy should produce a fever beyond 102 F

Other Forms of Pyretotherapy If for any reason malarial pyretotherapy cannot be carried out vaccine therapy or the use of the Kettering hypertherm or other forms of radiant heat may be substituted for it

bi 6 ars – 10 bi, 6 ars Some have preferred other schedules to this At present continuous treatment seems preferable to intermittent treatment with rest periods of no treatment Results should be tested periodically by serum reactions Ideally, treatment should be continued until serum negativity results these observations of the efficiency of the therapy should be made at intervals for at least 3 years

Iodides in Syphilis

With various forms of visceral syphilis, especially when gummas are present iodides are valuable as adjuncts to other anti syphilitic therapy Potassium iodide in the form of a saturated aqueous solution should be given in large doses given with milk its disagreeable taste is well concealed It should be begun in dosage of 0 6 gm (10 drops) 3 times a day, and increased gradually to 2 gm (30 drops) or more 3 times a day, in accordance with the patient's tolerance Some prefer sodium iodide to potassium iodide Iodide should be continued as long as clinical improvement takes place

Tryparsamide in Syphilis

Tryparsamide is the form of arsenic of particular value in the treatment of degenerative forms of syphilis of the central nervous system particularly general paresis in conjunction with or subsequent to, some form of pyretotherapy A recommended course of tryparsamide is 20 weekly intravenous injections of 0 3 gm each Because of possible toxic effects on the optic nerve the patient must be carefully watched for any evidence of them The toxic effects are indicated by the patient's reporting diminishing or blurred vision and shimmering lights before the eyes, by changes in the optic discs on oft repeated ophthalmoscopic examinations and by decrease in the size of visual fields as detected by perimetric measurements If these changes appear tryparsamide treatment must be stopped with possible resumption after the eyes return to normal It is usual to combine with the tryparsamide weekly intramuscular injections of bismuth subsalicylate in doses of 0 2 gm each as already described Along with tryparsamide many give penicillin as previously described

just described cannot be carried out, then substitute daily intramuscular injections of 600 000 units (2 cc) of aqueous procaine penicillin throughout the period of fever paroxysms or tri weekly intramuscular injections of 600 000 (2 cc) units of procaine penicillin with aluminum monostearate during the period of pyretotherapy A course of pyretotherapy is usually 8 to 10 paroxysms The results of such treatment and the need for repetitions are to be judged by oft repeated examinations of spinal fluid and by frequent clinical and psychiatric studies of patients with general paresis and taboparesis The same procedures except for psychiatric studies are to be used in patients with spinal fluid examinations and more important ophthalmoscopic and perimetric observations are to be given patients with primary optic atrophy For all of these except cases of optic atrophy if combined penicillin and pyretotherapy is not giving satisfactory improvement tryparsamide should be substituted for the penicillin It should be given in 20 weekly intravenous injections of 0 3 gm each

Treatment of Syphilitic Nerve Deafness and Erb's Spastic Paraplegia

In these forms of syphilis penicillin therapy alone as described in the preceeding section is preferred by many Others advise combining it with pyretotherapy This certainly should be done if the penicillin alone is not bringing about prompt and marked improvement

Prophylaxis With penicillin an effective dosage for prophylaxis against syphilis is 1 200 000 units in one treatment

YAWS

In recent years the treatment of yaws like that of syphilis has undergone a marked change Excellent results have been obtained from the use of penicillin A dose of 40 000 units intramuscularly every 3 hours until 3 000 000 units have been administered is recommended for the seriously ill patient with overwhelming infection For the usual case penicillin procaine in aqueous suspension or in oil with 2 per cent aluminum monostearate in a total dose of 1 200 000 units for adults 600 000 units for children under 12 and 900 000 units for children from 12 to 17 years divided into 2 injections given on consecutive days may be administered The results from penicillin therapy are dramatic In early yaws lesions and symptoms disappear promptly Chronic cases

For *vaccine therapy* an initial intravenous injection of 50 000 000 killed typhoid or mixed typhoid and paratyphoid (salmonella) bacteria is given followed by subsequent intravenous doses, the size determined by the fever-producing effect of the initial dose With proper dosage a temperature reaching 104°F can be maintained for 3 to 4 hours This should be repeated daily or every other day for a total of 8 to 10 fever periods

The *Kettering hypertherm* is an air-conditioned cabinet for the artificial induction of fever In it temperature, humidity and velocity of air have adequate and simple control With the Kettering hypertherm it is possible to elevate and maintain the body temperature of the individual in it at any desired physiological level When it is used in pyretotherapy it is customary to keep the patient's rectal temperature at 105° to 106°F as long as desired ordinarily for a period of 3 hours For general paresis and other forms of degenerative syphilis, these treatments are repeated twice weekly for 6 weeks Other schedules may be used in accordance with the patient s condition and reaction to the treatment In some clinics this form of pyretotherapy is believed to give better results than those obtained from malarial pyretotherapy

Pyretotherapy of any sort is inadvisable for patients with even moderately active tuberculosis poorly compensated heart disease, including any degree of syphilitic aortic insufficiency diabetes mellitus severe Bright s disease marked hepatitis or other conditions likely to be made worse by a course of pyretotherapy

Treatment of General Paresis Taboparesis, Tabes Dorsalis, and Syphilitic Primary Optic Atrophy

These are the forms of syphilis in which therapeutic results tend to be less satisfactory than in other forms of the disease chiefly because of the structure of the lesion which is predominantly degenerative in nature. In these forms success may depend on treatment being started at a very early stage in the process In them early diagnosis is of the utmost importance to satisfactory therapeutic results As soon as diagnosis has been made, pyretotherapy should be commenced without trial of penicillin alone, and with the first fever paroxysm penicillin should be begun in daily large dosage as follows preferably at least 100 000 units in aqueous solution given every 3 hours intravenously or intramuscularly and continued for 100 to 200 injections If the type of penicillin therapy

penicillin, the arsenicals, and bismuth It should be remembered, how ever, that spontaneous cure often occurs In mal de los pintos (pintas) the later pigment changes of the skin are unaffected by any therapy

Prophylaxis is best achieved by proper isolation of infected cases, personal and bodily cleanliness and *early recognition and treatment of* new cases Intramuscular bismuth as used in the treatment of syphilis, is thought by many to be preventive

BIBLIOGRAPHY

Syphilis

1 CURTIS A C, KITCHEN D K, O LEARY P A, RATTNER H, REIN C R, SCHOCH A G, SHAFFER L W and WILE, U J Penicillin Treatment of Syphilis *Jour Amer Med Assoc*, 1951 cxlv p 1223

2 STOKES J H, WOLFERTH C C, EDEIKEN J, FALK M S and FORD W T Treatment of Cardiovascular Syphilis *Jour Amer Med Assoc*, 1951 cxlvii p 944

3 WALKER S A and STOUGHTON R B Modern Trends in Syphilis Therapy *Med Clin No Amer* Jan 1951 p 143

4 WELSH H and LEWIS C *Antibiotic Therapy* The Arundel Press Washington D C 1951 p 304

respond rapidly, too, pain disappears and healing commences in skin and bone The serology, however is slow to change, and a high percentage of patients still have a positive serology 1 year after treatment

Aureomycin chloramphenicol, and terramycin are also effective against *Treponema pertenue* Darkfield studies show rapid disappearance of the treponema after oral dosage with these antibiotics and rapid healing of lesions As yet the most satisfactory dosage has not been found but excellent results should be obtained with an initial dose of 2 0 gm followed by 1 0 gm every 6 hours for 10 days

Chronic cases and cases requiring definitive treatment should receive additional treatment with arsenicals or bismuth In the tertiary stage a combination of penicillin and arsenical therapy, much as is employed in the treatment of syphilis, is recommended After the initial treatment with penicillin as just recommended mapharsen, 40 to 60 mg, or neoarsphenamine, 0 6 to 0 75 gm the smaller dosage being recommended for females given weekly in combination with bismuth salicylate, 0 2 gm for 4 weeks followed by 4 weekly injections of one of the arsenicals alone and terminated by 8 weekly injections of bismuth, should give excellent results even in the chronic well advanced cases

Melarsen oxide a stable trivalent compound, may be given intravenously daily for from 4 to 11 days as indicated in a dose of 25 mg This compound is stable even in the tropics, which much simplifies the treatment, and should prove valuable as a rapidly effective agent to curtail the ravages of this disease and decrease the sources of infection

For goundou and other ulcerative deforming lesions surgery, as indicated, will give relief

Prophylaxis

Mass chemotherapy markedly cuts down the spread of yaws Avoidance of contact with cases and careful protection of open wounds to prevent flies and other insects from contaminating them with yaws are essential Education of native populations and better sanitation are important in preventing the spread of yaws

Bejel and Mal de los Pintos

The treatment of these forms of spirochetal infection, particularly in the early stages, is as outlined for Syphilis They respond readily to

amount of fluid is to be determined on the basis of whether or not urine output is increased In many of these patients intravenous normal saline with 5 per cent glucose is indicated For the patient with marked oliguria and high level of non protein nitrogen, peritoneal infusion or the use of the artificial kidney as described for the treatment of uremia in the section on Bright s Disease may be needed to carry the patient over to a period of improved renal function and thus save his life The antibiotic therapy supplemented with cortisone in a dose of 200 to 300 mg a day may be helpful in carrying seriously ill patients over a period of crisis

The anemia of this form of leptospirosis if marked should be treated with blood transfusions and if moderate with ferrous sulfate or ferrous gluconate in doses of 0 3 to 0 6 gm 2 or 3 times a day preferably in enteric coated tablets.

Pre ention Workers who stand in or otherwise come in contact with water contaminated by the urine of rats dogs and other animals infected with *Leptospira ictero haemorrhagiae* or *L canicola* should be protected since this is the usual source of infection in this disease Contact with urine and possibly with feces of patients with infectious leptospiral hepatitis should be guarded against by disposal of urine and feces as described in the section on Typhoid Fever

Seven Day Fever

Treatment for this malady is essentially that described for Dengue *Penicillin may be helpful*

Prophylaxis Adequate protection from mosquitoes by netting chlorophenothane [DDT] dusting of areas screening and other mosquito control measures are essential to the prevention of the spread of this disease

Relapsing Fever Spirillum Fever or Borreliosis

These terms are used for a febrile disease caused by a number of species at least 6 of closely related spirella organisms now grouped in the genus Borrelia These can be grouped as (1) louse borne and (2) tick borne relapsing fevers All varieties should have the same form of treatment namely that appropriate to infectious diseases as described in Part 1 and specific therapy in the form of penicillin aureomycin chlor-

CHAPTER XVIII

LEPTOSPIROSIS AND BORRELIOSIS

Infectious Leptospiral Hepatitis Weil's Disease

This form of hepatitis in man is usually caused by *Leptospira ictero haemorrhagiae*, rarely by *Leptospira canicola*, the organism that infects dogs Clinically the disease is the same in man when caused by either of these organisms There are specific serological tests to identify the causative organism in a given case of human leptospiral hepatitis

Treatment with the patient kept in bed consists of using aureomycin or terramycin in an initial dose of 2 0 gm followed by 0 5 gm every 6 hours Results are not very satisfactory and in some cases this treatment may be without value Care must be exercised and the drug must be discontinued if there is no evidence of improvement or if there are any untoward effects Secondly measures to combat the symptoms derived from the lesions caused by the leptospira chiefly those in the liver and in more severe cases those in the kidney should be carried out Adequate supportive therapy as outlined in Chapter 1 is of utmost importance

The presence in the liver of the causative leptospiral organism causes varying degrees of hepatic insufficiency with as a rule, early jaundice This phase of the disease in addition to the use of antibiotics is to be treated as described for Viral Hepatitis, with the same insistence on prolonged avoidance of physical activity even after jaundice has cleared, if and when tests for liver function show persisting hepatic insufficiency

In the more severely ill patients there is usually renal insufficiency from leptospiral involvement of the kidney mainly of the lower nephron type, causing albuminuria oliguria and nitrogen retention In these patients aureomycin should be continued for its effect on the spirilla, since it seems not to increase renal insufficiency These patients should receive a diet restricted in protein in proportion to the degree of elevation of the blood non protein nitrogen and containing ample fluid, the

amount of fluid is to be determined on the basis of whether or not urine output is increased In many of these patients intravenous normal saline with 5 per cent glucose is indicated For the patient with marked oliguria and high level of non protein nitrogen, peritoneal infusion or the use of the artificial kidney as described for the treatment of uremia in the section on Bright s Disease may be needed to carry the patient over to a period of improved renal function and thus save his life The antibiotic therapy supplemented with cortisone in a dose of 200 to 300 mg a day may be helpful in carrying seriously ill patients over a period of crisis

The anemia of this form of leptospirosis if marked should be treated with blood transfusions and if moderate, with ferrous sulfate or ferrous gluconate in doses of 0 3 to 0 6 gm 2 or 3 times a day preferably in enteric coated tablets

Prevention Workers who stand in or otherwise come in contact with water contaminated by the urine of rats dogs and other animals infected with *Leptospira ictero haemorrhagiae* or *L canicola* should be protected since this is the usual source of infection in this disease Contact with urine and possibly with feces of patients with infectious leptospiral hepatitis should be guarded against by disposal of urine and feces as described in the section on Typhoid Fever

Seven Day Fever

Treatment for this malady is essentially that described for Dengue Penicillin may be helpful

Prophylaxis Adequate protection from mosquitoes by netting, chlorophenothane [DDT] dusting of areas, screening and other mosquito-control measures are essential to the prevention of the spread of this disease

Relapsing Fever Spirillum Fever or Borreliosis

These terms are used for a febrile disease caused by a number of species at least 6 of closely related spirella organisms now grouped in the genus Borrelia These can be grouped as (1) louse borne and (2) tick borne relapsing fevers All varieties should have the same form of treatment namely that appropriate to infectious diseases as described in Part 1 and specific therapy in the form of penicillin aureomycin chlor-

CHAPTER XVIII

LEPTOSPIROSIS AND BORRELIOSIS

INFECTIOUS LEPTOSPIRAL HEPATITIS WEIL'S DISEASE

This form of hepatitis in man is usually caused by *Leptospira ictero haemorrhagiae*, rarely by *Leptospira canicola*, the organism that infects dogs Clinically the disease is the same in man when caused by either of these organisms There are specific serological tests to identify the causative organism in a given case of human leptospiral hepatitis

Treatment with the patient kept in bed consists of using aureomycin or terramycin in an initial dose of 2 0 gm followed by 0 5 gm every 6 hours Results are not very satisfactory and in some cases this treatment may be without value Care must be exercised and the drug must be discontinued if there is no evidence of improvement or if there are any untoward effects Secondly measures to combat the symptoms derived from the lesions caused by the leptospira, chiefly those in the liver and in more severe cases those in the kidney should be carried out Adequate supportive therapy as outlined in Chapter 1 is of utmost importance

The presence in the liver of the causative leptospiral organism causes varying degrees of hepatic insufficiency with as a rule early jaundice This phase of the disease in addition to the use of antibiotics is to be treated as described for Viral Hepatitis with the same insistence on prolonged avoidance of physical activity even after jaundice has cleared, if and when tests for liver function show persisting hepatic insufficiency

In the more severely ill patients there is usually renal insufficiency from leptospiral involvement of the kidney mainly of the lower nephron type, causing albuminuria oliguria and nitrogen retention In these patients aureomycin should be continued for its effect on the spirilla, since it seems not to increase renal insufficiency These patients should receive a diet restricted in protein in proportion to the degree of elevation of the blood non protein nitrogen and containing ample fluid, the

spira, penicillin should be tried as described for the treatment of Yaws, or aureomycin should be tried as for Weil's Disease

BIBLIOGRAPHY

Leptospirosis and Borreliosis

1 BATCHELOR T M and TODD G M 'Aureomycin and Penicillin Therapy in Leptospirosis (Weil's Disease) *Jour Amer Med Assoc* 1950 cxliii p 21

2 BRAINERD H D LENNETTE E H MEIKLEJOHN G BRUYN H B Jr and CLARK W H Symposium on Antibiotics the Clinical Evaluation of Aureomycin *J Clin Invest* 1949 xxviii p 99

3 HALL H E HIGHTOWER J A DIAZ RIVERA R BYRNE R J SMADEL J E and WOODWARD T E Evaluation of Antibiotic Therapy in Human Leptospirosis *Ann Int Med* 1951 xxxv p 981

4 HEILMAN F R Aureomycin in the Treatment of Relapsing Fever and Leptospirosis Ictero haemorrhagic (Weil's Disease) *Proc Staff Meet Mayo Clinic* 1948 xxiii p 569

amphenicol or terramycin given as described for syphilis The anti biotic to be used should be determined by in vitro tests against the infecting organisms

Prevention This consists of protection against lice as described in the section on Typhus so far as the louse-borne group is concerned and against ticks so far as the tick borne group is concerned Protection against ticks is difficult, since these arthropods do not live on man but in the floors or walls of native houses, in cracks in the floors and walls of caves and in the burrows of various small animals, whence they usually come out at night to feed on the human host From these places it is not easy to eradicate them Infested native houses may have to be destroyed Known places of infestation should be avoided for camp and housing sites Any observed ticks on body or clothing should be killed promptly but not by squeezing them with bare hands

Rat-bite Fever

There are two varieties of rat bite fever, one caused by *Streptobacillus moniliformis*, the other by *Spirillum minus* The treatment of the former variety is described under Haverhill Fever

Rat bite fever caused by *Spirillum minus* should be treated by bed rest and a nutritious easily digested diet with sufficient fluid intake to give a 24-hour urine output of not less than 1500 cc Penicillin as prescribed for Pneumococcus Pneumonia should be given as soon as the diagnosis is made This failing, streptomycin should be started in parenteral dosage of 1 0 to 2 0 gm daily and continued until the temperature has been normal for 4 days, unless severe toxic symptoms develop In that event another antibiotic should be used, preferably aureomycin in dosage described for the treatment of Virus Pneumonia.

Prevention Rats and mice should be eradicated as completely as possible from the house barn, stable, and any other infested building since they often harbor *Spirillum minus* even though they appear healthy

Other Leptospiroses

These diseases include *swamp fever* of eastern Europe *autumn fever* or *hasmi* in Japan and a disease resembling Dengue found in Java and in Argentina As each is caused by a different species of the genus Lepto

There are available several reasonably effective chemical amebacides each having some special merit As antibiotics also seem to be effective against amebae however it is possible that they may replace the chemical amebacides

Chemical Amebacides

The chemical amebacide or combination of them chosen for use depends somewhat on the preference of the clinician since several of them are equally effective Acute cases exhibiting diarrhea should be kept in bed and should receive emetine hydrochloride intramuscularly 1 mg per kilogram per day or as is commonly found satisfactory 60 mg for 6 days provided there is no heart liver or kidney disease and the patient is not pregnant Emetine is the drug of choice in the presence of diarrhea and is capable of rapidly clearing up the diarrhea as well as the other symptoms of the acute cases It is however not a very effective amebacide and consequently should be supplemented with one of the more effective drugs if after its use the stools are still positive for amebae as they most commonly will be As emetine can and does exhibit a toxic effect on the heart and other organs it is wise to be alert to prevent any possible damage Electrocardiograms taken before and during the course of therapy usually after 0 3 gm have been given at the completion of treatment and one week afterward will detect early changes These changes consist essentially of abnormalities in the T waves Other signs of toxicity are increased diarrhea fatigue dyspnea on exertion muscular tremors and weakness At the first sign of any toxic effect emetine must be discontinued and one of the drugs named below substituted During the administration of emetine after the diarrhea has abated chiniofon U S P should be given by rectum For this purpose it is given as a retention enema of 1 to 5 gm freshly dissolved in 200 cc of water daily for 8 to 10 days

Immediately after the last dose of emetine hydrochloride vioform in enteric coated capsules 0 5 gm twice daily for 12 days or diodoquin 1 5 to 2 0 gm in divided doses daily for the same period of time is recommended If vioform or diodoquin is not available or cannot be employed emetine bismuth iodide 0 2 gm daily for 12 days or carbarsone U S P 0 25 gm twice daily after meals for 10 days is recommended as second choice Care must be taken to avoid the use of these drugs in the presence of severe liver or kidney damage As they contain iodine the

CHAPTER XIX

AMEBIASIS

Experience gained in treating amebiasis in various parts of the world and under different conditions has shown that as yet there is no rapid completely effective specific medication, but that a combination of good supportive treatment and the amebicidal drugs now available gives excellent results The general measures outlined in Part 1 should be instituted promptly once the diagnosis is made If there is fever, severe diarrhea, or marked emaciation and blood loss, the patient must be put to bed, placed on a nourishing low residue diet, receive intravenously physiological salt solution, plasma and if necessary, blood If diarrhea is severe, aluminum hydroxide or kaolin aluminum hydroxide mixtures (Kaomagma) 15 cc 1 hour before meals may be given If necessary morphine sulphate 8 mg and atropine sulfate 0 5 to 1 0 mg, may be given hypodermically for colic and diarrhea If constipation becomes a feature magnesium hydroxide (milk of magnesia), 15 cc, is indicated Many patients have the milder form of the disease and can be treated on an ambulatory basis except during the period of emetine therapy, when to meet promptly possible cardiotoxic effects it is wiser to enforce bed rest

In acute cases the diet should be liquid consisting of boiled milk whey broths, soft boiled eggs toast tea and gelatin This should be well supplemented with vitamins, especially C and B Chronic cases may have a much more liberal diet high in calories protein, and vitamins but low in carbohydrate It should be a smooth non irritating diet of low residue Highly spiced and seasoned foods are to be avoided, as are leafy vegetables and unstrained fruit juices

Bowel discharges, bed linen eating utensils and other personal articles should be handled as described under Typhoid Fever However in comparison to carriers and convalescent cases there is little danger of spread from an acutely ill patient

Antibiotics

As already intimated it is possible that the antibiotics will prove effective against amebae and will be preferred to the amebicides just mentioned Reports indicate that several of the antibiotics are effective in killing amebae in the intestinal tract Reports of their use in numerous cases however especially with extensive follow up studies are needed before the best way to use them will be known The relapse rate is higher than with other amebicidal agents This important question must be settled by clinical study So far several antibiotics have been shown to be effective against amebae and have cured amebiasis in patients Aureomycin bacitracin and terramycin are effective Aureomycin and terramycin should be given in a dose of 1 0 gm every 6 hours for 15 days Bacitracin should be given in an oral dose of 80 000 to 120 000 units daily for 2 weeks Patients with extensive intestinal tract ulceration should be closely observed for possible renal damage and bacitracin is not recommended for use in children in patients with renal disease or for an amebic abscess in the liver

Criteria of Cure If the stools are negative at the completion of the course a period of 2 weeks should elapse and then microscopical examination of the stool on 6 consecutive days should be made If these and a sigmoidoscopic examination are negative the case may be considered cured

Treatment of Complications

Cases with complications such as amebic hepatitis amebic abscess of the liver lung brain or other organ hemorrhage and perforation of the bowel should receive emetine as already outlined in addition to such specific therapy as may be indicated to alleviate the situation Surgery penicillin or other antibiotic or the sulfonamides either alone or in combination are essential in many of these complicated cases Emetine should be given a complete trial before more drastic procedures are undertaken since it will often obviate further measures It is wise to avoid open drainage of amebic abscesses especially of the right lobe of the liver where more favorable results may be obtained by repeated aspirations Hepatic abscess cases should be observed carefully and if fever pain and increased white blood cell count develop after an aspiration they signify that drainage should be continued not that

untoward effects of iodides in tuberculosis and iodide sensitivity cases must be remembered

Carbarsone may also be given as a retention enema If given as an enema it should either replace oral medication with the drug or be given at a different time As a retention enema 2 gm of the drug is dissolved in 200 cc of warm 2 per cent sodium bicarbonate solution and administered after a cleansing enema with a 1 per cent solution of sodium bicarbonate Retention enemas should be given every other night for a maximum of 5 enemas Sedation with pentabarbital (Nembutal), 0 1 gm, or secobarbital (Seconal), 0 1 gm is recommended Administration of carbarsone must be stopped promptly if there are any signs of idiosyncrasy or arsenical toxicity such as gastro-intestinal irritation jaundice neuritis or skin eruption, the toxic action should be controlled by the use of dithiopropanol (BAL) as described under Arsenic Poisoning

Thioarsenites (Thiocarbasone) seem even more effective and less toxic than the drugs just mentioned They are given by mouth to adults in a dose of 100 mg 3 times a day for 10 days Children should receive 4 to 6 mg per kilogram of body weight per day given in divided doses It may also be given by rectum in a dose of 0 5 to 1 0 gm daily for 6 days Children should receive proportionately smaller doses

Bismuth glycolylarsanilate (Milibis), more recently introduced is also a valuable agent for the treatment of amebiasis It is given to adults in a dose of 0 5 gm 3 times a day for 7 days There is very little danger of acute toxicity with this drug but the factor of arsenic or bismuth sensitivity must be considered

Since there is often an associated bacillary dysentery and certainly an infection of the amebic ulcers, especially in chronic cases with bowel damage considerable improvement may be obtained by the use of oral sulfadiazine 4 gm initially followed by 1 gm every 4 hours Sulfasuxidine or sulfathalidine 1 to 3 gm given orally is also helpful

The course of treatment must be checked carefully by repeated stool examinations If the stool shows cysts or active amebae the treatment must be repeated Emetine however should not be repeated for at least one month Carbarsone (Thiocarbarsone) or (Milibis) followed by a repeat course of vioform or diodoquin is recommended The chronic cyst passer with symptoms should be treated as already outlined If cyst infected stools alone are found and there are no symptoms a course of vioform or diodoquin followed by carbarsone (Thiocarbarsone) or (Milibis) as already described is indicated Emetine is not to be given

3 MOST H and VAN ASSENDELFT F Laboratory and Clinical Observations on Effect of Terramycin in the Treatment of Amebiasis *Am J Trop Med* 1951 xxxi p 284
4 WILMOT A J ARMSTRONG T G and ELSDON DEW R Comparative Value of Amoebicidal Drugs, *Am Jour Trop Med and Hygiene London* 1951 LIV p 161

therapy has failed An abscess in the left lobe of the liver is more difficult to aspirate properly, and it is usually necessary to employ drainage through an abdominal incision Owing to the frequency of secondary bacterial invasion the use of penicillin and/or other antibiotic in full doses, is indicated in cases with abscess formation The choice depends on the type of invading organism and its sensitivity to the antibiotics.

Prophylaxis Because of the widespread distribution of *Endameba histolytica* cysts great care must be taken to prevent contamination of food and water Since carriers are a constant source of spread of the disease, they must be kept from handling food until their stools are free from cysts Rigid rules for sanitary food handling and personal hygiene of food handlers will do much to prevent the spread of the disease Any food handler who has a diarrhea or possible infection should have a stool examination before being permitted to return to work In this way many carriers can be found and the potential danger eliminated When there is doubt regarding sanitation food should be thoroughly cooked and drinking water boiled Flies must be prevented from depositing cysts on food after it is cooked since they are a potent source of transmission. Sewage must be handled in such a manner as to prevent contamination of food or water either directly or by flies In heavily infested areas water should be boiled or sterilized with more than the usual amounts of chlorine Care must be used in sterilizing water with chlorine as the cysts are very resistant Tincture of iodine 0 2 cc or succinchlorimide N F 12 mg per liter, left in the water for at least 30 minutes, may be employed If the water is turbid or contains much organic matter, it should be boiled

Individuals exposed to infection can prevent development of the disease by taking diiodohydroxyquinoline (Diodoquin), 0 4 gm 3 times a day by mouth for periods up to 3 weeks Aureomycin in a dose of 1 0 to 2 0 gm daily is also helpful in preventing infection

BIBLIOGRAPHY

Amebiasis

1 BARGEN J A Present day Management of Amebiasis" *Jour Amer Med Assoc*, 1951 CXLV p 785

2 HALL W H Treatment of Chronic Human Amebiasis with Aureomycin *N E J Med*, 1951 CCXLIV, p 495

From this it follows that the clinical course of malaria in an individual will be conditioned in a definitive manner by the species of plasmodium involved since different strains have different life histories in the human host are characterized by different immunological responses and respond differently to therapy There are also species differences for each strain of vivax malaria has its own characteristic pattern of periodicity There are likewise differences in strains in their response to treatment

Finally immunological factors modify the course of a malarial infection In general the longer a particular attack of malaria has lasted before the institution of treatment the less drug is required for a favorable therapeutic result Similarly, relapses respond better to treatment than does the initial attack

Since most of the effective drugs in use until recently for the treatment of malaria have their action chiefly on the erythrocytic phase of the disease they readily cure the acute attacks and are very useful in suppressing attacks but do not give permanent cures Recently an 8 amino quinoline derivative (Primaquine) has been found effective against the tissue phase Its use combined with the use of a drug effective against the erythrocytic phase has given a high percentage of cures

The Acute Attack

The patient with an acute attack of malaria should be confined to bed at least until the disease is brought well under control as indicated by freedom from symptoms and normal temperature He should be given a highly nutritious diet and fluids forced to balance those lost by sweating, fluids should be given parenterally if there is dehydration During the chill the patient may be made more comfortable by wrapping him in woolen blankets and applying hot water bottles or a heating pad For the headache that is so common acetylsalicylic acid 0 6 gm every 2 to 4 hours is usually sufficient Nausea may be lessened by 2 0 to 4 0 gm sodium bicarbonate in a glass of warm water The anemia caused by the disease should be treated with iron preparations Transfusions may be used but are seldom necessary

The Choice of Drug This depends in part upon the causative organism and in part on what is to be accomplished with drugs Quinacrine (Atabrine) chloroquanide (Paludrine) and chloroquine (Aralen) are most effective for *P falciparum* strains So far none of these is curative

CHAPTER XX

MALARIA AND BLACKWATER FEVER

Malaria

The treatment of malaria depends upon the following six factors (1) the nature of the infection as it pertains to treatment, (2) the acute attack, (3) suppressive treatment (4) transfusion malaria, (5) induced malaria, (6) prophylaxis

Nature of the Infection

Following the extensive research on malaria in World War II, it is now believed that instead of entering directly into the red blood cells of a human, sporozoites from a mosquito first enter fixed tissue cells They then undergo a development phase characterized by more than one cycle with reinvasion of other fixed tissue cells After several such cycles forms of the parasite capable of invading and growing in the red blood cells develop and initiate an erythrocytic phase of the disease

It is thought that both *Plasmodium vivax* and *P falciparum* undergo both tissue and erythrocytic phases of the disease but that they differ particularly in their tissue phases this accounts for their differences in response to treatment The fixed tissue phase which may persist for a long time, causes no signs or symptoms In vivax malaria this primary tissue phase becomes a persisting tissue phase from which parasite forms capable of invading red blood cells are developed from time to time, initiating the erythrocytic cycles that are responsible for the clinical attacks of malaria and the relapses

In the falciparum infection the tissue phase does not seem to persist far beyond the establishment of the erythrocytic phase of the disease Continuation of falciparum malaria appears to depend solely on the persistence of the erythrocytic phase, as the infection never relapses when adequately treated

6 days should be given There usually occurs only one more chill after the drug is instituted and the fever subsides in 24 to 48 hours At the end of the week's course 0 1 gm daily for an additional month will produce radical cure in falciparum malaria Because of the hypothetical fixed tissue stage of parasites in *P vivax* malaria this form of the disease tends to relapse on an average of 4 to 6 weeks after the drug is stopped although the relapse rate is somewhat less and the interval between relapses longer than after quinine therapy Its action has proved to be equivalent to that of quinine in vivax malaria and superior in falciparum malaria

Quinacrine may be used intramuscularly for the very ill patient or for *P falciparum* infections in doses of 0 2 gm in 5 0 cc distilled water This may be repeated in 6 hours with oral dosage commenced as soon as possible

The principal toxic effects of quinacrine are gastric disturbances psychoses and a lichenoid dermatitis Nausea occurs rather commonly during the first few days of administration but subsides spontaneously It may be avoided by giving the drug with meals with a full glass of water or with sweetened tea or fruit juice Mental disturbances are rare but true psychoses may occur with mental confusion disorientation and mania or stupor Visual and auditory delusions and hallucinations may occur The symptoms are relieved by stopping the drug Uniformly the drug causes a yellow discoloration of the skin and sweat which produces no symptoms and is not to be considered a toxic manifestation Under tropical conditions a lichen planus like eruption may become manifest this subsides in most instances by withdrawing the drug and removing the patient to a temperate climate

The treatment for a relapse with quinacrine is the same as the initial treatment

Chloroquine Phosphate U S P (Aralen Diphosphate) A German synthetic product this was developed during World War II but was not put to any extensive field trials by our armies Although more potent than quinacrine it likewise does not prevent the infection or cure the disease It is more rapidly absorbed considerable quantities are deposited in the organs and tissues allowing for a lower dosage schedule and effective lower plasma concentrations It clears the blood stream of parasites more quickly and reduces the febrile period faster than either quinine or atabrine The relapse rate after chloroquine is about the same as with the other two drugs but the parasitic latent period after termination of treatment (the period between relapses) is usually much

for *P vivax* or *P malariae*, although they are highly successful in terminating the acute attack and in suppression When they are combined with the new 8 aminoquinoline derivative (Primaquine), cures are obtained These drugs differ widely in their toxicity

Quinine Quinine the oldest specific therapy for malaria, is still preferred by some It is highly effective but does not bring the acute attack under control as quickly as does quinacrine or chloroquine, and the relapse rate is slightly higher and the interval between relapses shorter than with either of the other two drugs Its chief disadvantage is its toxicity (cinchonism) particularly when used on a large scale, with symptoms of nausea, vomiting tinnitus, headache, and vertigo These do not contraindicate the drug but the occurrence of idiosyncracy with urticaria dyspnea, cyanosis, and collapse calls for immediate withdrawal of quinine

For control of the acute attack quinine sulfate is usually given by mouth, 1 0 gm 3 times a day for 2 days then 0 6 gm 3 times a day for 5 days In a malarious area this should be followed by suppressive treatment In patients severely ill with *P vivax*, and especially in those with *P falciparum*, quinine dihydrochloride 0 6 gm dissolved in 300 cc of physiological saline solution, to which has been added 1 0 cc of 1 1000 epinephrine solution may be given intravenously If these are not available quinine hydrochloride may be given intramuscularly, 0 2 gm dissolved in 3 0 cc sterile distilled water Such parenteral injections may be repeated at 6 hour intervals, with oral dosage begun as soon as possible

Quinine has been implicated as a possible cause of blackwater fever and its use is advised against in that condition

The treatment for a relapse is the same as the treatment just outlined for an initial attack

Quinacrine Hydrochloride U S P (Atabrine, Mepacrine) This is a synthetic drug a quinoline derivative (3 chlor 7 methoxy 9-1-methyl 4-diethyl aminobutylamino-acridine dihydrochloride) Although at first many considered it not as good as quinine and more toxic, the experiences and research of World War II proved this drug effective for the treatment of acute attacks of malaria Its efficacy depends upon the plasma concentration of the drug, best results being obtained with a relatively large priming dose followed by a maintenance dose for nearly a week. It is curative against the asexual parasite of *P falciparum* For either benign tertian (*P vivax*) or malignant tertian (*P falciparum*) strains, 0 2 gm every 6 hours for 5 doses followed by 0 1 gm 3 times a day for

quinine has not seemed to enhance the value of either in the treatment of malaria

The toxic dose of chloroguanide is approximately 200 times the therapeutic dose so the drug is relatively harmless Dosages over 1 0 gm a day may give rise to gastro intestinal disturbances such as vomiting, abdominal pain and diarrhea and to urinary symptoms, including hematuria Occasionally granular and hyaline casts may appear in the urine Chloroguanide does not stain the skin The symptoms usually subside promptly when the drug is discontinued

The treatment for a relapse with chloroguanide is the same as that outlined above for an acute attack

Primaquine, an 8 aminoquinoline [8 (4 amino-1 methylbutylamino)-6 methoxyquinoline] is one of the newer compounds effective in destroying the tissue stages of the disease and in that sense is more curative of the infection On the other hand it has little effect on the erythrocytic forms responsible for the relapse but by its action on the tissue stages can prevent the development of these forms It has been used most successfully in the Korean (temperate zone) strain of *P vivax* malaria and is effective in relatively small doses It has also been found to be effective in the tropical (Chesson) strain of *P vivax* malaria but larger doses may be required Because of the lessened effectiveness of primaquine on the erythrocytic forms, it should be combined with chloroquine in treating an acute attack of malaria When these are given in combination a quick remission occurs and the relapse rate has been found to be nearly zero For this purpose chloroquine (Aralen) 0 3 gm every 8 hours for the first 24 hours followed by 0 3 gm daily for 2 days and primaquine 15 mg daily for 14 consecutive days are given The curative dose of primaquine may vary between 10 and 30 mg daily depending upon the degree of immunity of the individual the density of the organism inoculum and the species strain The tropical (Chesson) strain of *P vivax* may require the full 30 mg daily

Although the spread between effective and toxic dosage is relatively great primaquine particularly in the larger doses may cause abdominal cramps anorexia nausea vomiting burning epigastric distress and more seriously *toxic effects on the bone marrow* hemolytic anemia leukocytosis leukopenia and granulopenia especially in Negroes With hematopoietic toxicity the drug should be stopped and transfusions given as indicated The abdominal symptoms may be lessened by giving primaquine with a meal

longer, often twice as long as with quinine and quinacrine Chloroquine is generally less toxic Clinical cures of *P vivax* malarial attacks are readily obtained with it but relapses are not prevented Like quinacrine it will effect a complete cure of malignant tertian *(P falciparum)* malaria

For the acute attack of malaria an initial dose of 1 0 gm of chloroquine followed by an additional 0 5 gm in 6 to 8 hours, then by a single dose of 0 5 gm on each of two consecutive days is recommended This regime eradicates infection due to *P falciparum* and terminates the acute attack of *P vivax* infection

The toxic symptoms of chloroquine parallel those of quinacrine but are much milder the drug does not cause yellow discoloration of the skin The symptoms of mild and transient headache, visual disturbances, pruritus and gastro intestinal disturbances are the most common, but they readily disappear on stopping the drug It does not cause an eczematoid reaction (lichen planus) of the skin but there may be slight transient pruritus

The treatment for a relapse with chloroquine is the same as that outlined above for the acute attack

Chloroguanidine Hydrochloride U S P (Paludrine) An English synthetic drug developed during World War II, this was found to be an effective agent in the treatment of both *P vivax* and *P falciparum* malaria in man It does not appear to act as rapidly as quinine or chloroquine but will cause fever to subside and plasmodia to disappear from the blood stream When given in the proper dosage, it is a true causal prophylactic for falciparum malaria giving complete protection against this parasite This is distinctly an advantage over the other drugs and it is the drug of choice in treating *P falciparum* malaria The dosage for prophylaxis of *P falciparum* infection is 0 1 gm twice a week A single dose of 0 3 gm a week will suppress both *P falciparum* and *P vivax* malaria The curative dose for falciparum malaria is 0 1 gm 3 times a day for 10 days For vivax malaria the same dosage may be employed but complete cure does not result and clinical improvement may be considerably slower than that after administration of quinacrine or chloroquine The latent period after chloroquanide is usually longer than that after quinine and only slightly shorter than that after quinacrine The latent period may be considerably less than that following chloroquine

The experimental concurrent administration of chloroguanide and

Chloroquine phosphate (Aralen), for suppressive treatment, should be given in doses of 0.25 gm to 0.50 gm once a week, on the same day each week.

Chloroguanide hydrochloride (Paludrine), for casual prophylaxis of *P falciparum* infections should be given in doses of 0.1 gm twice weekly. A single dose of 0.3 gm once a week is usually effective in suppressing clinical symptoms and parasitemia of both malignant and benign malaria.

Curative Treatment

Except for *P falciparum* malaria prompt cures of malaria were not obtainable until recently. This was especially true of *P vivax* malaria. Quinine, quinacrine, chloroquine and chloroguanide all give cures of *P falciparum* malaria when given in sufficient dosage for a long enough period of time. Until recent years only pamaquine and pentaquine in combination with quinine gave any cures with *P vivax* malaria. Recently primaquine shows real promise of giving a high percentage of cures of *P vivax*.

Pentaquine phosphate is similar in its pharmacology and action to pamaquine (Plasmochin). Given in combination with quinine, pentaquine lowers the relapse of vivax malaria. It is less toxic than pamaquine but care must be exercised in giving it to Negroes since it is more toxic for dark-skinned people. It should not be given in the presence of renal lesions or concurrently with sulfonamides or other antimalarial drugs except quinine.

The chief value of pentaquine curative treatment is to individuals who leave endemic for nonmalarious regions or to persons residing in only slightly or moderately malarious regions who have reason to believe that the chance of new infection is not likely to be great.

For curative therapy in primary attacks of vivax malaria pentaquine should be administered in doses of 30 to 60 mg with 1.0 to 2.0 gm of quinine daily for 14 days; for relapses 30 mg daily with 2.0 gm of quinine a day for 14 days is usually effective. With this dosage the only side reactions are occasional abdominal cramps, methemoglobinemia (seldom) and rarely leukopenia or acute hemolytic anemia. All patients who are to receive pentaquine therapy should be under close supervision, preferably in a hospital.

Suppressive Treatment

The purpose of suppressive therapy is to impair the ability of parasites of the erythrocytic phase to reproduce themselves and so increase in number as to be able to evoke clinical symptoms of the underlying disease In falciparum malaria the continuation of suppressive therapy by any one of the regimes already described for the treatment of the acute attack should result in fairly prompt cure, provided, at the same time the patient is removed from the hazard of a further infection In vivax malaria this is not the case, and relapses are to be expected the number and time of occurrence being dependent upon the strain of the offending organism, the density of the initial infection, and the time during the course of the disease that treatment is terminated

The indications for the use of suppressive therapy are (1) during periods of malarial exposure and preferably for 4 weeks thereafter, ( ) following a clinical attack, if general debility exists, and (3) before, during, and after any medical, surgical, or obstetrical crisis, if an individual is known to have an underlying infection with *P vivax*

As with the treatment of the acute attack the effectiveness of suppressive therapy depends in large part upon the maintenance of a level of the drug in the blood stream adequate for suppression All of the drugs already outlined under treatment are effective but the most recent studies favor chloroquine (Aralen) or chloroquanide because of the smaller doses necessary, the less frequent administration needed, and their less toxic effects

Quinine sulfate, if used may be given in doses of 0 3 to 0 6 gm daily, continued for 4 to 8 weeks after any exposure to mosquitoes has been precluded Symptoms of nausea and tinnitus are common Some people cannot tolerate the drug

Quinacrine hydrochloride (Atabrine) has been found from the experiences of World War II to be very effective in doses of 0 1 gm daily Before entering a malarious area it is wise to build up a blood level either by priming doses of 0 1 gm 3 times a day for several days and then a maintenance dose of 0 1 gm daily, or by giving 0 1 gm daily for 2 weeks After 3 or 4 weeks of this dosage the skin develops a yellow color, which may remain 2 or 3 months fading gradually after the drug is stopped During the war careful investigation of cases that developed despite such a scheme of suppressive treatment revealed in most instances that the drug had not been taken faithfully, day in and day out

Transfusion Malaria

At the present time it is thought that this form of malaria contracted usually by accident differs from the mosquito borne disease in that the fixed tissue stage of the infection does not occur Since this form tends to remain more localized as an erythrocytic stage it is much easier to eradicate and permanent cure usually results The drugs and dosage to be used are the same as those already outlined under Acute Attack

What may be termed *drug addict malaria* the infection resulting from the common use of an apparatus for the administration of morphine or heroin intravenously belongs in the same category *P falciparum* is usually the organism and it causes a high mortality rate For the cerebral or severe gastro intestinal forms of this type of malaria the patient should be given quinine dihydrochloride 0 6 gm in 10 cc of physiological saline solution every 3 to 4 hours day and night for 24 hours Fluids 2000 to 5000 cc parenterally as 5 per cent glucose in saline with 10 mg of thiamin chloride per liter should be given daily With anemia jaundice hematuria shock or low plasma proteins transfusions of 500 cc of whole blood should be administered If coma persists 50 cc of spinal fluid should be withdrawn and 50 cc of 50 per cent glucose with 1 0 cc of 1 10 000 epinephrine solution added should be given intravenously The latter procedure may be repeated in 6 hours if necessary A daily enema should be given

With clinical improvement usually by the second day the quinine injections may be given only every 6 to 8 hours limiting the intravenously given quinine to 4 days Nourishment by mouth should be begun as soon as possible Usually no attempt should be made to withhold heroin or morphine until the patient is convalescing from the malaria

When the clinical manifestations have improved sufficiently chloroquine by mouth should be given in the dosage recommended for acute malaria attacks This should be supplemented by a high vitamin high calorie diet intramuscular liver extract 1 0 cc daily ferrous sulfate 0 6 gm or ferrous gluconate 0 6 gm 3 times a day and vitamins Drug withdrawal should be commenced only after the patient has entirely recovered

If gametocytes remain in the blood stream after the treatment outlined above has been completed the patient may be given pantaquine pamaquine or primaquine as described under Curative Treatment

In less severe or simple or latent cases of falciparum malaria in drug

A less toxic drug than pentaquine is a newer product, isopentaquine. As yet there is insufficient data to assess ... malaria therapy.

Pamaquine (Plasmochin) is a German synthetic antimalarial ... on the fixed tissue stage of the malarial parasite ... and is effective primarily against the ... peripheral blood. Pamaquine and quinine are usually given ... produce the curative effect described under pentaquine. ... and the dosage may need to be varied depending ... of plasmodia, it must be given in adequate dosage for ... period of time. A usual dose has been 90 mg of pamaquine ... gm of quinine sulfate daily for 14 days. This dosage ... unpleasant side effects. Studies of this drug during World War II demonstrated that frequently 30 mg with 2.0 gm of quinine ... daily for 14 days produces satisfactory results in vivax malaria.

Pamaquine is to be used in selected recurrent cases of malaria in cases that persistently reveal sexual forms of the parasite (gametocytes) in the peripheral blood after an adequate course of quinine or chloroquine. It renders a patient with falciparum malaria non-infectious to mosquitoes. Pamaquine should not be used with quinacrine, ... a very high pamaquine plasma level results and continues for a ... period of time. It may be used after quinacrine, however, if an interval of 2 or more days has elapsed.

The chief toxic symptoms of pamaquine are abdominal discomfort, pain, ... cyanosis, and methemoglobinemia. They rarely necessitate termination of therapy. Acute hemolytic anemia and shock may occur, more commonly among dark skinned people than among Caucasians. The anemia begins on the second to fourth day of therapy and is to be considered a medical emergency, calling for cessation of the drug and prompt administration of whole blood. A toxic syndrome resembling blackwater fever has been described with abdominal pain, dark urine, anorexia, nausea, vomiting, fever, weakness, jaundice, and backache; it is thought to result from intravascular hemolysis. Such poisoning should be treated vigorously with rest, a high fluid and high carbohydrate intake. Transfusions of whole blood are important if the anemia is severe or if shock is impending.

Primaquine, 15 mg daily for 14 days, combined with chloroquine, 0.3 gm every 8 hours for 24 hours and then 0.3 gm a day for 2 days, is curative in a high percentage of malaria cases infected with *P. vivax* and *P. falciparum*.

Drugs also need to be considered in prophylaxis The suppressive action of quinine quinacrine, chloroquine and chloroguanide is also a prophylactic measure, as already outlined under Suppressive Treatment

Blackwater Fever

This is the most serious sequel of malaria its exact etiological relation to the malarial parasite is unfortunately not clearly understood It usually follows malaria caused by P *falciparum*, although at times it may appear as a sequence to other varieties of malaria According to almost all malariologists the antimalarial drug that is being given should be stopped as soon as there is evidence of blackwater fever and not recommenced until convalescence is established Bed rest is imperative with a simple fluid and semi solid diet Fluid intake should be large 2000 to 6000 cc as needed to secure a urine output of 1200 to 1500 cc Parenteral fluid is usually needed perferably an alkaline one such as 5 75 gm sodium chloride and 18 25 gm sodium bicarbonate in 1000 cc of distilled water the sodium bicarbonate being added to the sterilized solution containing sodium chloride this should be given every 12 hours if vomiting is severe and urine is highly acid or scanty Blood trans fusions are advisable After convalescence chloroquine quinacrine (Atabrine) or other non quinine antimalarial should be given Removal of the patient during early convalescence from the malarious district preferably to a temperate climate is advisable

BIBLIOGRAPHY

Malaria

1 LINTS H COATNEY G COOPER W COLWELL W WHITE, W and EYLES D Studies in Human Malaria Prolonged Suppression of Chesson Strain Vivax Malaria by Weekly Administration of Chloroquanide or Chloroquine *Jour Nat Malaria Soc* 1950 ix p 50

2 McLENDON S B and YOUNG M D Response of Plasmodium Malariae Infections to Three Different Drugs *Jour Amer Med Assoc* 1951 cxlvii p 822

3 MULTIPLE AUTHORS Symposium on Malaria *J Clin Invest* 1948 xxvii p 2

A less toxic drug than pentaquine is a newer member of the series, isopentaquine. As yet there is insufficient data to assign its place in malaria therapy.

Pamaquine (Plasmochin) is a German synthetic antimalarial which acts more on the fixed tissue stage of the malarial parasite than quinine or quinacrine and is effective primarily against the gametocyte in the peripheral blood. Pamaquine and quinine are usually given together to produce the curative effect described under pentaquine. Pamaquine is quite toxic and the dosage may need to be varied depending upon the strain of plasmodia, it must be given in adequate dosage for a long enough period of time. A usual dose has been 90 mg. of pamaquine with 2.0 gm. of quinine sulfate daily for 14 days. This dosage usually produces unpleasant side effects. Studies of this drug during World War II demonstrated that frequently 30 mg. with 2.0 gm. of quinine sulfate daily for 14 days produces satisfactory results in vivax malaria.

Pamaquine is to be used in selected recurrent cases of malaria and in cases that persistently reveal sexual forms of the parasite (gametocytes) in the peripheral blood after an adequate course of quinine, quinacrine, or chloroquine. It renders a patient with falciparum malaria non-infectious to mosquitoes. Pamaquine should not be used with quinacrine, as a very high pamaquine plasma level results and continues for a long period of time. It may be used after quinacrine, however, if an interval of 2 or more days has elapsed.

The chief toxic symptoms of pamaquine are abdominal discomfort or pain, leukopenia and methemoglobinemia. They rarely necessitate the termination of therapy. Acute hemolytic anemia and shock may occur, more commonly among dark-skinned people than among Caucasians. The anemia begins on the second to fourth day of therapy and is to be considered a medical emergency calling for cessation of the drug and prompt administration of whole blood. A toxic syndrome resembling blackwater fever has been described with abdominal pain, dark urine, anorexia, nausea, vomiting, fever, weakness, jaundice, and backache; it is thought to result from intravascular hemolysis. Such poisoning should be treated vigorously with rest, a high fluid and high carbohydrate intake. Transfusions of whole blood are important if the anemia is severe or if shock is impending.

Primaquine, 15 mg. daily for 14 days combined with chloroquine 0.3 gm. every 8 hours for 24 hours and then 0.3 gm. a day for 2 days, is curative in a high percentage of malaria cases infected with *P. vivax* and *P. falciparum*.

CHAPTER XXI

COCCIDIAL, TOXOPLASMAL, SARCOSPORIDIOSIS AND TRYPANOSOMAL DISEASES

Coccidiosis

Treatment for this rare malady, which must not be confused with coccidioidomycosis is the same as that used against parasitic worms of the intestinal tract Fortunately most cases are apparently self limiting and cause few symptoms Bed rest and an adequate diet are all that are usually needed The use of sulfonamides and the wide spectrum antibiotics is advised for resistant or complicated cases and for those exhibiting secondary infections

Prophylaxis Prevention consists essentially in adequate sanitary measures to prevent contamination of food and water Thorough cooking of food and boiling of water are indicated where contamination is likely, as in tropical and subtropical areas Proper sterilization of drinking water as described under Amebiasis will prevent infestation from contaminated water

Sarcosporidiosis

There is no known effective treatment for sarcosporidiosis The disease causes few or no symptoms rarely there may be some debility from muscular wasting

Although the epidemiology is not well understood it is thought that the infection is acquired from food or water contaminated with feces containing the spores of the parasite consequently feces of known cases should be sterilized as described under Typhoid Fever

Toxoplasmosis

There are three clinical forms or types of toxoplasmosis (1) acquired

addicts the treatment given under Acute Attack should be instituted, using either chloroquine or chloroguanide

In either type relapse and especially reinfection with the needle are common Such cases should be placed under the jurisdiction of the local health department

Induced Malaria

The susceptibility of different individuals to an induced attack of malaria, particularly in the production of fever for the treatment of syphilis of the central nervous system varies considerably chiefly with race Large numbers of the Negro race cannot be infected by this means because of either previously acquired immunity or a natural immunity Hence such individuals who do not develop the disease after inoculation require no active treatment It is thought that those who do develop the paroxysms of chills and fever do not develop the fixed tissue stages of the disease as discussed under Transfusion Malaria, attacks are likewise quite readily terminated Very frequently the disease burns itself out after a dozen or so paroxysms and no treatment is required On the other hand it is customary after the required fever therapy to administer quinine 0 3 gm 3 times a day for 7 to 10 days, or chloroquine in the usual doses Relapse is uncommon

Prophylaxis

The function of prophylaxis is to prevent the acquisition of a malarial infection by an individual and at the same time to prevent the further transmission of the malaria to mosquitoes To be effective the measures instituted must be continued without interruption as long as an individual remains in endemic malaria regions The steps to be taken require consideration of both the community and the individual For the community, eradication of anophelene mosquitoes is the prime requisite, oiling the surface of the water and periodic spraying of the area (by airplane) with 5 per cent chlorophenothane [DDT] will help to eliminate the breeding places For the individual adequate protective clothing, the proper application of repellents (dimethylphthalate) to the exposed parts, the spraying of Chlorophenothane in the living and sleeping quarters each evening and the rigid utilization of mosquito netting are fundamental

be done immediately to ascertain any central nervous system involvement this should be repeated at intervals during the treatment and at least twice at six month intervals after completion of treatment

Specific therapy with one of the arsenicals should be instituted promptly Melarsen oxide gives excellent results This should be given orally in mild early cases in a dose of 3 mg per kilogram of body weight for from 5 to 8 consecutive days This route is recommended however only when it is impractical to give the drug intravenously When possible all cases certainly the more advanced ones and those with central nervous system involvement, should receive the drug daily in intravenous dosage of 0 1 mg per kilogram of body weight for 7 consecutive days The intravenous route is the route of choice in most cases and will give much better results than the oral route This drug is stable even under tropical conditions and consequently has much to recommend it

Pentamidine also gives excellent results in early cases It should be given intravenously in a daily dose of 0 1 gm for 10 to 20 doses If toxic signs appear the drug should be stopped *Phenylarsenoxide*, a recently employed compound is also effective in early cases It should be given by mouth in a dose of 6 to 7 mg per kilogram of body weight daily for 7 days If the patient is in bad physical condition 0 5 mg per kilogram of body weight should be given daily for 14 days A high percentage of complete cures have resulted from this therapy In advanced cases and those with central nervous system involvement it is wise to supplement phenylarsenoxide with tryparsamide

Tryparsamide is best given intravenously in distilled water in a dose of 40 to 50 mg per kilogram of body weight The initial adult dose should be 1 0 to 1 5 gm the subsequent doses depend on the patient s weight and should be between 2 0 to 3 0 gm for 15 weekly injections Patients receiving any arsenical drug must be observed carefully for any signs of toxicity this is especially true when giving tryparsamide as there is a narrow margin of safety between the therapeutic and the toxic dose Visual fields should be checked before during and after a course of treatment in order to detect any early changes Photophobia excessive lacrimation ocular pain or dimness of vision may be an indication of developing optic atrophy and at the appearance of any one of these the drug should be stopped and dithiopropanol (BAL) administered as described under Arsenic Poisoning Tryparsamide is the drug of choice for this disease when there is central nervous system involvement

4 SHANNON J A Recent Advances in Malaria," *Postgrad Med*, 1948, III p 171
5 STRAUS B and GENNIS J 'Radical Cure of Relapsing Vivax Malaria with Pentaquine Quinine" *Ann Int Med*, 1950 XXXIII, p 1413
6 Council on Pharmacy and Chemistry Report on Status of Primaquine *Jour Amer Med Assoc*, 1952 CXLIX p 1558

60 mg per kilogram of body weight for adults 60 to 90 mg for children, and 100 to 120 mg for infants, especially those with the meningoencephalitic form of the disease Treatment should be continued without interruption until the blood is free of the parasites and the general symptoms disappear The injections cause pain and, frequently, fever but these are not serious and treatment should be continued Urinary tests for albumin should be taken before each injection Only at the appearance of albuminuria is interruption of therapy advisable After albuminuria has disappeared treatment can be resumed without danger in equal or even higher doses The additional use of Neostibosan or Solustibosan appears to show little benefit Penicillin may be useful and a daily dose of 600 000 units of penicillin procaine should be given intramuscularly A new arsenical Bayer 9736 shows some promise and may be tried Should cardiac failure or arrhythmias develop they should be treated as described under those headings Spontaneous recovery does occur

Prophylaxis Avoid native abodes or thatched huts in endemic areas Protective netting is effective since the vector bug feeds at night A light burning in the sleeping quarters also tends to repell the bug Screening and spraying with Chlorophenothane [DDT] is effective

(2) congenital, and (3) chronic or latent The acquired form usually and the congenital form frequently appear as severe acute infections, very often with high mortality Some of the congenital cases, however, have only mild early symptoms or even none at all, but later show the signs of latent or chronic toxoplasmosis such as intracranial calcification and/or marked eye signs chronic hydrocephalus, retarded speech development mild mental deficiency and convulsions

Treatment of all forms of toxoplasmosis is unsatisfactory The patient with the acquired or congenital form with symptoms of a severe acute infection must be in bed receiving the general treatment described in Part 1 The sulfonamides sulfadiazine, or sulfamerazine, in full dosage for at least 2 or 3 weeks should be used Penicillin, so far as it has been tested seems to be ineffective against the toxoplasma organism Other antibiotics have not been evaluated Emetine hydrochloride 20 to 60 mg daily for 10 days may be helpful Unfortunately, although the sulfonamides suppress the parasite the over all results of treatment are not good

The latent form needs no therapy The chronic form should be treated symptomatically If there are convulsive seizures, treatment should be as described for Epilepsy

In chronic active toxoplasmosis the development of localized hypersensitive reactions to the organism may be a serious factor in the disease Patients with active chorioretinitis with the disease have responded favorably to desensitization by gradually increased doses of toxoplasma antigen Pyretotherapy may supplement the desensitization treatment For this purpose typhoid vaccine given intravenously as recommended for pyretotherapy in syphilis may be used Cortisone may also prove helpful

Prophylaxis Since the epidemiology of toxoplasmosis is not understood, no effective prophylactic measures can be advised

African Trypanosomiasis

The first measure in the treatment of this disease is to begin at once to build up general resistance The supportive measures as outlined in Part 1 should be instituted The patient should be placed in a screened room to prevent further infection from flies A nourishing diet containing abundant vitamins and sufficient fluid to reverse any dehydration is to be given, the fluid either orally or by vein Lumbar puncture should

Small children should receive less pentavalent antimony than that given to larger children and adults but in general they tolerate antimony better than adults

Refractory cases resulting from a resistant strain or from drug fastness from previous treatment with an antimony preparation should be given the aromatic diamidines The preparation of choice is 4 4' diamidino stilbene (Stilbamidine) which should be given intravenously as a freshly prepared 1 per cent solution in distilled water The initial dose should be 25 mg which should be increased by 10 to 20 mg until the patient is getting a daily dose of 1 0 mg per pound of body weight A minimum of 10 injections totaling 0 75 gm of the drug per 100 pounds of body weight is required Usually there is a prompt improvement temperature falls and the spleen rapidly decreases in size The drug is highly toxic and care must be taken in its use Reactions occur in nearly all individuals treated These consist of headache flushing epigastric pain vomiting collapse and unconsciousness Hydroxyamphetamine (Paredrine) hydrobromide 20 to 40 mg by mouth before injection is protective as is epinephrine hydrochloride 0 5 cc of a 1 1000 solution subcutaneously After a course of treatment is completed, there should be a rest period of at least 1 month

If the anemia is marked it should be treated with blood transfusions followed by liver extract and ferrous sulfate or gluconate With moderate anemia blood transfusions may be omitted

Prevention The sandfly *(Phlebotomus argentipes)* is the usual vector Consequently their destruction or the guarding of man against their bites is most important in prophylaxis The dog also can be host to the causative *Leishmania* particularly in the infantile form and so possible infection from that source must be guarded against In man with kala azar the *Leishmania* may be excreted in stools and urine as well as in nasal or mouth discharges and they may be present in discharging skin lesions To guard against these sources of infection all of the discharges should be sterilized by heat or chemically Bed linen dressings and eating utensils should be boiled promptly after use Those caring for a kala azar patient should protect themselves by thoroughly washing their hands after all contact with the patient

Oriental Sore Delhi Boil

This lesion caused by cutaneous leishmanial infection responds well to several therapeutic measures Extensive lesions should be treated as

Suramin sodium U S P (Naphuride) also is effective and was used widely before the advent of the newer agents just discussed The initial dose recommended is 0 3 to 0 5 gm freshly dissolved in 10 cc of distilled water and given intravenously If there are no untoward effects the dosage should then be increased to 1 0 gm Injections should be given at 4 day intervals until a total dose of 10 gm has been given The patient must be observed carefully for toxic effects There may be an immediate circulatory collapse or because of the tendency of suramin to accumulate toxic levels that will damage the kidney may be reached This drug should not be given if renal disease is present, or if albu minuria dermatitis chills, fever, headache, pruritus, or other signs of toxicity appear

Prophylaxis Adequate therapy for infected cases aids greatly in preventing spread of the disease Screening of dwellings and other build ings is essential in endemic areas The wearing of suitable clothing, in cluding long sleeves and long trousers, affords protection Care must be taken to destroy tsetse flies in vehicles boats and airplanes coming from infected areas Where practicable spraying with chloropheno thane, [DDT] 2 to 3 pounds per acre and the use of 5 per cent powder in vehicles boats and airplanes will destroy most flies In areas where animals are infected, it may be necessary either to destroy them or to leave the area until the insects are brought under control

Suramin (Naphuride) 1 0 gm for adults 0 3 to 0 75 gm for children and 0 15 to 0 2 gm for infants given intramuscularly, repeated in 1 week and followed by the same dose every 3 months is of value in individual prophylaxis Melarsen oxide orally 3 mg per kilogram of body weight, once every month or two is also valuable as a prophylactic agent

South American Trypanosomiasis Chagas' Disease

The several drugs that have been found to be effective in the treat ment of the various stages of African trypanosomiasis, such as suramin sodium (Naphuride) tryparsamide, pentamidine and phenylarsenoxide are of no value in the therapy of the South American form of the disease

A quinoline derivative, the sulfate of diallyl malonyl diamide of 2 methyl 4 6 diamino quinoline (Bayer 7602) has been reported as giving good results in eliminating *T cruzi* from the body and clearing up the morbilliform schizotrypanide' eruptions It is employed best as a 3 per cent solution given deep intramuscularly in daily doses of 30 to

under Kala-azar with several additions because of the location and character of the lesions Careful screening of the patient with fine mesh netting should be carried out as protection against sandflies Bed rest together with a highly nutritious diet including vitamins and adequate fluids should be instituted as outlined in Part 1 For the more severe cases pentavalent antimony compounds such as Neostibosan, Neostam urea stibamine, Solustibosan and Stilbamidine may be used intravenously as described under Kala azar It is thought by some that the older drug antimony and potassium tartrate [tartar emetic], given 3 times a week intravenously is just as effective as the newer preparations in the cutaneous form of the disease In the adult the dose begins with 1 0 cc of a 2 per cent solution 30 mg, increasing ½ cc every third or fourth injection until by the twelfth week the patient is receiving 0 12 gm in 6 0 cc of 2 per cent solution 3 times a week Intolerance to the drug may require modification of this schedule A total treatment of 3 months is usually sufficient Tartar emetic is about 20 times more toxic however than the newer pentavalent antimony preparations producing such symptoms as headaches fever cough nausea vomiting, diarrhea and occasionally lymphadenitis

Local therapy for the mucocutaneous lesions may be carried out as for cutaneous leishmaniasis This may include scraping of the lesions followed by local infiltration of the edges of an ulcer with 1 or 2 cc of 5 or 10 per cent quinacrine (Atabrine) hydrochloride solution or the application of 10 per cent Atabrine ointment Non infected lesions may be infiltrated with a . 0 per cent solution of Neostam or berberine sulfate 20 cc of a 1 per cent solution may be injected into the tissues about the ulcer once a week As an adjunct sodium arsenite 5 mg 3 times a week or 10 mg given intradermally twice a week has been recommended

Prophylaxis Prevention of mucocutaneous leishmaniasis consists in elimination of the breeding places of sandflies and the protection against them with the use of insect repellents such as chlorophenothane [DDT] the wearing of protective clothing against insect bites and the careful utilization of fine meshed screening in doors and windows and about the bed Some work has been done in immunization by inoculating material from moist skin lesions into human subjects although some success has been claimed for this the disadvantage is that it may take a year for immunity to develop during which time the subject is susceptible to the disease

CHAPTER XXII

LEISHMANIAL DISEASES

Kala-azar

The patient with kala azar, with its unusually long continued fever, its hypoproteinemia and anemia, needs bed rest and prolonged nursing care and especially a protein rich, high calorie, vitamin rich diet in addition to an antimony preparation It is well to give supplemental vitamins also The general management should be very like that recommended for pulmonary tuberculosis in its febrile stage Stomatitis should be treated with an alkaline mouthwash (N F) and the measures recommended for stomatitis under Typhoid Fever

Antimony has a specific action against the causative *Leishmania* and should be given to all kala-azar patients The trivalent antimony, sodium antimony tartrate which was previously used, has been almost entirely replaced by the pentavalent antimony compounds because they are less toxic to the host and more effective against the causative *Leishmania*

Any one of the following pentavalent antimony drugs may be used ethyl stibamine (Neostibosan) stibamine glucoside (Neostam), or urea stibamine, others are under trial, some of which may prove better All of the three mentioned should be given intravenously in the form of a 5 per cent solution in freshly distilled water Ethyl stibamine (Neostibosan) should be given intravenously usually on alternate days sometimes daily in a gradually increasing amount commencing with 0 2 gm and rising to 0 3 gm per 100 pounds of body weight, these injections should be continued until a total of 3 0 gm has been given to a patient weighing 100 pounds more or less proportionately for larger or smaller patients Stibamine glucoside (Neostam) and urea stibamine should be given intravenously or when necessary intramuscularly, in an initial dose of 0 05 gm gradually increased to 0 2 or rarely 0 25 gm per 100 pounds of body weight Injections should be made on alternate days and continued until a total of 2 5 to 3 0 gm per 100 pounds of body weight has been given

2 HILL L M WRIGHT, L T PRIGOT A and LOGAN M A Aureomycin in Granuloma Inguinale *Jour Amer Med Assoc* 1949 cxli p 1047
3 MACKIE T HUNTER C and WORTH C *A Manual of Tropical Medicine* W B Saunders Co Philadelphia 1945 p 170
4 MARSHAK I C and RODRIGUEZ J Granuloma Inguinale Treatment with Streptomycin *Jour Amer Med Assoc* 1948 cxxxvii p 1293
5 MAZZA S Tratamiento de las Inferonadad de Chages *Prensa Med Argentina* 1941 xxviii p 1579
6 ROBINSON H M Jr Recent Advances in Diagnosis and Treatment of Granuloma Inguinale *Ann Int Med* 1947 xxvii p 1046
7 WEINMAN D and FRANZ K Early Results of the Treatment of African Trypanosomiasis with Two New Arsenical Preparations *Am J Trop Med*, 1945 xxv p 343

described under Kala-azar Local, well-circumscribed lesions may be controlled by x-ray Carbon dioxide snow (dry ice), applied locally for from 5 to 30 seconds, depending on the extent of the sore, and repeated at intervals of approximately 10 days until healing is evident, has proven effective

Berberine sulfate, 2 per cent solution, injected through a fine needle and infiltrated into the indurated area surrounding the base of the ulcer, is effective though painful Usually 1 0 cc divided in 6 weekly injections is required for each ulcer

The local lesions also respond well to systemic therapy with drugs such as ethyl stibamine (Neostibosan) which is so effective in visceral leishmaniasis This is to be given slowly intravenously as a 5 per cent solution For adults and children over ten years of age the initial dose is 0 2 gm, increased to 0 3 gm during the course of 8 to 12 injections which are given on alternate days The total dose rarely should exceed 3 5 gm Younger children may be given 0 05 to 0 1 gm increased to 0 2 gm during the course of 8 injections given on alternate days Usually, the total dose should not exceed 1 0 gm

Toxic reactions are not as common with ethyl stibamine (Neostibosan) as with older antimony preparations and with stibamine glucoside (Neostam), but neostibosan is definitely contraindicated in the presence of jaundice, hepatitis, nephritis pneumonia ascites or heart disease

Since the cutaneous lesions are usually infected with secondary bacterial invaders, sulfadiazine in full dosage or penicillin, streptomycin, or other antibiotic, depending on the sensitivity of the organism and therapeutic response is indicated Local application of an ointment of these potent antibacterial substances or the use of tyrothricin or bacitracin ointment may result in rapid healing this treatment should at least bring about striking improvement by controlling secondary invaders

Prophylaxis Protection from sandflies avoidance of contaminated areas the use of insect repellants, and the dusting of areas with insect poisons are the most important factors in preventing this disease Vaccination is apparently worthy of trial for individuals likely to be exposed

Mucocutaneous Leishmaniasis

The treatment of the mucocutaneous form of the disease, also spoken of as American Leishmaniasis is essentially the same as that outlined

suppositories of the drug should be inserted deep into the vagina every second night in the intervals between intensive treatment Usually a course of 3 intensive treatments with it is effective These should be scheduled to carry the patient through 3 menstrual cycles The patient must be observed carefully for signs of arsenic toxicity, and at the first indication of local or systemic reaction the drug must be discontinued.

The pH of the vaginal fluid during the course of treatment and for some time afterward should be kept on the acid side by the insertion of lactose tablets and by douches of lactose and water at least twice a week One teaspoonful of pure lactic acid to a quart of water makes an excellent douche solution

Silver picrate as a 1 per cent powder (Powder Picragol Compound), also is an excellent trichomonocide After cleansing with tincture of green soap and drying, the vagina is dusted once a week with 5 gm of 1 per cent silver picrate powder and a suppository of 2 per cent silver picrate (Vaginal Suppositories Picragol) is inserted nightly This treatment continued for 3 weeks usually gives good results Douches must be avoided during the period of treatment Lactic acid suppositories should be inserted often enough to maintain acid vaginal secretions

During the course of treatment coitus should be avoided Treatment should be scheduled so that intensive therapy is given just after the menstrual period, since it is at this time that the trichomonas are most active If there is considerable itching and burning glycerin suppositories inserted deep in the vagina will give some relief

Many simple remedies give temporary relief and in a fair percentage of milder cases apparently arrest the infection These consist of daily douching with 25 per cent sodium chloride solution or daily douching with lactic acid douches (one teaspoonful of pure lactic acid to a quart of water) The antibiotic aureomycin used as a powder in a dose of 0 5 gm in 20 gm of talc applied every other day for 5 applications also shows promise Chloramphenicol terramycin bacitracin and tyrothricin also have trichomonocidal activity and show promise in the treatment of this disease Vaginal suppositories containing diodoquin (Floraquin), 2 suppositories inserted twice daily may be used Bismuth glycolylarsanilate (Milibis), 0 25 gm vaginal suppositories or Tampax with Milibus containing a 0 25 gm tablet attached to the tip and 0 15 gm of the powder dispersed in the cotton of the ordinary vaginal Tampax tube are effective and simple to employ

Granuloma Inguinale

This disease formerly treated with antimony compounds, is now being treated more satisfactorily with aureomycin, chloramphenicol, terramycin streptomycin or dihydrostreptomycin given in the usual doses Streptomycin or dihydrostreptomycin both requiring parenteral dosage and having a considerable toxicity should be the antibiotics to use after the others effective by mouth have been tried in a given case and found to be ineffective More extensive observation is needed before it can be stated whether aureomycin, chloramphenicol, or terramycin will be the antibiotic of choice in treating granuloma inguinale

If an antibiotic cannot be given recourse should be had to one of the antimony compounds Several of these are available Antimony and potassium tartrate if used should be given intravenously as a 1 per cent solution in doses of 0 03 to 0 12 gm 3 times a week for 3 weeks

Less toxic than this preparation are stibophen U S P (Fuadin), antimony thioglycollamide and antimony sodium thioglycollate Stibophen should be given intramuscularly in an initial dose of 1 5 cc of a 6 3 per cent solution followed by 3 5 cc on the second day and 5 0 cc every other day until a total of 40 cc has been given In a week or two following healing the course may be repeated Antimony thioglycollamide should be given intramuscularly in a dose of 0 08 gm dissolved in 20 cc of sterile water every second day for 15 to 25 injections Antimony sodium thioglycollate should be given intramuscularly in doses of 0 05 to 0 1 gm dissolved in 10 to 20 cc of sterile water every third or fourth day until 15 to 25 injections have been given After these doses of antimony one such dose weekly for 4 months is advised to prevent relapse

Until the surface lesions heal sterilized dressings should be used Sometimes thorough surgical excision is necessary

BIBLIOGRAPHY

Leishmanial Diseases

1 FRENKEL J Pathogenesis Diagnosis and Treatment of Human Toxoplasmosis *Jour Amer Med Assoc* 1949 CXL p 369

the parasite has been eliminated the patient should have a high calorie, high-vitamin diet in order to regain weight

BIBLIOGRAPHY

Trichomoniasis

1 McVAY L LAIRD R FLANAGAN J and SPRUNT D The Treatment of Trichomonas Vaginalis Vaginitis with Aureomycin, *Proc Soc Exp Biol and Med* 1949 LXXII p 674

CHAPTER XXIII

PARASITIC INFUSORIA

TRICHOMONIASIS

Infection with *Trichomonas*, while usually not severe, can be annoying and resistant to treatment. Effort should be directed toward general improvement in health: a high calorie, high-vitamin diet and adequate rest, both physical and mental, are advised. If anemia is present, iron should be given.

Before commencing therapy, careful microscopic check of the vaginal fluid, urinary sediment and feces in the female, as well as of the urinary sediment and prostatic fluid of the husband, should be made in order to ascertain, if possible, the source of the infection. Since from 5 to 10 per cent of males harbor the parasite in the lower genito-urinary tract, usually without symptoms, that source of infection must be considered.

Infection in the gastro-intestinal tract may be a possible source of vaginal infection and should be treated with bismuth glycolylarsanilate, carbarsone, diodoquin, or vioform given in the same dosage and manner as advised for amebic infections. Vaginal infection responds readily to a variety of treatments, but unfortunately none of them is entirely successful in securing a complete eradication of the infection. Excellent initial results are often followed by a recurrence of symptoms. Methods designed to lower the pH of vaginal fluids to 4.5 or 4.0, together with trichomonocidal therapy, produce the best results.

Specific therapy should be initiated by careful cleansing of the introitus, urethral meatus, and vaginal wall, with special care to cleansing all the folds and the cervix, with tincture of green soap. The parts should then be dried with cotton or gauze swabs. One glass tube containing 0.5 gm. of phenarsone sulfoxylate (Aldarsone) and 2.5 gm. of kaolin should then be applied to every part of the cervix, vagina and introitus. This treatment should be repeated on 3 consecutive days,

PART VII

DISEASES DUE TO METAZOAN PARASITES

CHAPTER XXIV

DISEASES DUE TO FLUKES AND CESTODES

Hemic Distomatosis Schistosomiasis Bilharziasis

Schistosoma infection of the blood vessels leading to widespread tissue damage in the bladder, lower intestine liver, lung, rectum, and many other organs may present a difficult and serious therapeutic problem Bed rest is indicated in serious cases Patients should be given a high caloric diet, rich in vitamins especially vitamins B C and K If evidence of liver damage is present the treatment outlined for Cirrhosis should be instituted Anemia should be treated with adequate amounts of iron as described under Secondary Anemia If there is considerable gastro intestinal irritation a bland form of iron such as iron gluconate, should be used

The bladder lower intestinal tract and rectum may need local treatment for infection polyps and calculi For bladder infections antibacterials as described for cystitis are indicated Polyps should be excised when it is feasible and certainly when there is ulceration and mechanical interference Removal of calculi will of course give much relief. Large fibrotic spleens causing mechanical difficulties should be removed Occasionally ileostomy may be necessary in a thickened non functioning colon in which the mucosa is largely destroyed

If ascites is present as a result of cirrhosis, it should be treated as described under Decompensated Cirrhosis

Specific therapeutic measures when administered early give reasonably good results In chronic cases, however they are not so effective

Balantidiasis

Treatment to clear the stools of balantidia should be with carbarsone, chiniofon or Vioform tried in this order These drugs come as enteric coated pills tablets or gelatin capsules Each drug is to given by mouth with meals 2 or 3 times a day, for a period of 10 days Each dose should be 0 25 gm Additional courses of treatment, with intervening rest periods of 10 days may be necessary for a cure

Prevention is by avoiding contact with pigs, particularly with their dung

Giardiasis

The presence of *Giardia lamblia* in the intestinal tract, particularly in the duodenum, may cause intermittent diarrhea or low grade dysentery on the other hand its presence may be coincidental, causing no symptoms whatever The latter case has caused some authors to state that giardiasis requires no treatment Nevertheless, its potentiality in causing recurrent diarrhea, disturbances of the liver and gall bladder, chronic malnutrition from lack of proper absorption of nutrients from the intestinal tract and even bronchiectasis warrants attempts to eradicate it from the bowel

Quinacrine (Atabrine) hydrochloride has been found to be quite specific In World War II a course of atabrine was given for giardiasis, just as it was used for acute malaria, and results were excellent This regimen consisted of 0 2 gm every 6 hours for 5 doses, then 0 1 gm 3 times a day for 6 days In civilian practice on the other hand, 0 1 gm 3 times a day for 5 days has produced splendid results For children the dosage may be proportionately smaller, up to 5 years 0 1 gm daily, from 5 to 12 years, 0 2 gm daily 12 years and over, the adult dose, 0 1 gm 3 times a day

Since the first course of treatment may not completely eradicate the organisms from the intestinal tract two more courses may be given with an interval of one week between them

If quinacrine hydrochloride is not tolerated, mercurochrome in enteric coated capsules may be used 0 1 to 0 2 gm 3 times a day for 2 weeks Carbarsone or diodoquin in the same dosage as recommended for amebiasis are also effective

If the infection has caused any degree of inanition or wasting, after

China and India There are several varieties of flukes capable of producing liver involvement in man namely clonorchis opisthorchis and fasciola Although presenting similar clinical findings they vary somewhat in their response to therapy

Treatment should be initiated by placing the patient on a high calorie high protein high carbohydrate low fat diet supplemented with abundant vitamins especially B complex C and K Patients with anemia should receive iron If a macrocytic anemia is present liver or vitamin B_{12} given parenterally is recommended Serious cases with severe anemia should receive transfusions to build up blood and general resistance Clonorchiasis and opisthorchiasis in their early stages are helped by the administration of methyl rosaniline chloride (gentian violet) The initial dose should be 20 cc of a 1 per cent solution given intravenously and followed 3 days later by 30 cc Gentian violet may also be given orally as 1½ hour enteric coated tablets 60 mg 3 times daily before meals for 4 weeks

Sodium antimony tartrate as a freshly prepared 2 per cent solution may be given intravenously in an initial dose of 60 mg increased in subsequent doses given on alternate days so that by the third injection 0 12 gm is being used A total dose of 1 3 to 1 8 gm is usually sufficient The patient should be recumbent before and during injections and for at least one hour thereafter Dimercaprol injection (BAL in oil) should be available in case toxic reactions occur and should be administered as described under Arsenic Poisoning Diphenhydramine (Benadryl) hydrochloride 50 to 100 mg given orally one hour before injections may help avert reactions

In chronic cases where there is considerable liver damage and cirrhosis is a complicating factor the patient should be given treatment to combat it.

Fascioliasis should receive the same general supportive measures as outlined for clonorchiasis and opisthorchiasis The only drug of any apparent value is emetine which should be administered as described under Amebiasis Cirrhosis and hepatic decompensation should receive the therapy outlined for these conditions

INTESTINAL DISTOMATOSIS FASCIOLOPSIASIS

Specific treatment for intestinal flukes is reasonably satisfactory and when it is combined with supportive measures excellent results are obtained

3 weeks If there is evidence of kidney damage magnesium sulfate should be used with caution and sodium phosphate or the much less palatable sodium sulfate substituted

Pulmonary Distomatosis Paragonimiasis Parasitic Hemoptysis

Treatment for *Paragonimus westermanni* infection of the lung is not very satisfactory To combat emaciation, anemia and general weakness the general measures described for intestinal and hepatic distomatosis are indicated Penicillin streptomycin, or other antibiotics and the sulfonamides are indicated if there are complicating infections Emetine hydrochloride administered as described under Amebiasis is recommended Potassium antimony tartrate may prove helpful A fresh 2 per cent solution is given in an initial dose of 3 0 cc followed by 4 5 cc on the third day and increased to 6 0 cc on the fifth day Injections should be continued on alternate days until a total dose of 1 3 to 1 8 gm has been given Patients should be recumbent during and for at least one hour after administration of the drug if toxic symptoms appear the dose should be reduced and the intervals between doses increased Whenever possible the patient should leave the epidemic zone In the absence of reinfestation recovery may occur, owing to the death of the parasites

Prophylaxis Preventive measures against the various flukes consist in avoiding contaminated water for bathing or drinking, in not eating fresh vegetables or uncooked foods especially fresh water fish and sheep livers contaminated with flukes in the destruction of snails with copper sulfate 1 200 000 and in drainage of infected water Education of natives is important and installation of sanitary privies or where possible sewage drainage to swift streams is recommended Mass therapy is also effective in some situations All food consumed in endemic areas must be thoroughly cooked and water must be chlorinated before consumption

Intestinal Cestodes Tapeworms

For the treatment of tapeworms an anthelmintic drug is given to paralyze or kill the worm so that it is detached from its place in the intestine and subsequently expelled by catharsis The head of each worm should be identified in the stool as evidence that treatment has been

since the tissue damage already present is the main difficulty Antimony preparations have proved effective

Stibophen (Fuadin) is effective and is administered intramuscularly as a 6 3 per cent solution Adults should receive an initial dose of 1 5 cc, 3 5 cc the next day, and then 5 0 cc on alternate days until 10 doses have been given If eggs of the parasite are still present, the course of treatment may be repeated after 2 weeks Occasionally 3 courses are necessary to eliminate the infection For children the initial dose should be 0 5 cc, followed by 9 doses of 3 5 cc

If stibophen is ineffective, a course of the more effective potassium or sodium antimony tartrate may be given, but care must be exercised in patients with severe renal, hepatic cardiac, or central nervous system disease For this treatment a 2 per cent solution is prepared and sterilized by bringing it to the boiling point twice Then it is slowly administered intravenously on alternate days or 3 times a week An initial dose of 2 0 cc increased by 1 0 cc at each injection to a dose of 6 or 7 cc, depending on the patient's tolerance, is recommended If coughing, nausea vomiting or joint pain appears the dose is toxic and should be reduced to one that does not produce these symptoms A total dose of at least 2 0 gm is recommended This requires 16 to 18 injections over a period of 5 or 6 weeks If toxic effects appear, dimercaprol and antihistaminics may prove helpful

Lithium antimony thiomalate (Anthiomaline), a newer antimony preparation has proved effective and may be given intravenously or intramuscularly as a 6 per cent solution in a dose of 2 0 cc on alternate days for 10 injections The intravenous route is preferable, and the total dose should not exceed 1 3 gm

A new non antimony compound of much lower toxicity, 1 methyl 4 b diethyl-aminoethyl aminothioxanthone (Miracil D), has been devel oped It shows good action against *S haematobium* but apparently much less against *S mansoni* A dose of 60 mg per kilogram of body weight given over a period of 6 days is recommended

If antimony preparations are ineffective emetine may be given a trial It is administered as described for the treatment of Amebiasis

Hepatic Distomatosis Clonorchiasis, Fascioliasis, and Opisthorchiasis

Infestation of the liver by various flukes although rare in the United States is a common disease in certain areas of the world, notably Japan

cosis, careful washing should follow any handling of these worms their eggs, and the stools containing them

Somatic Teniasis

Cysticercosis There is no specific treatment If cysts cause pressure symptoms, surgical removal is indicated, if possible Prevention depends on precautions against auto infection with eggs of *T solium*, the usual cause of cysticercosis

Echinococcosis Hydatid Disease For this there is no effective drug If the cyst is large and troublesome or if it is infected surgical incision with evacuation of contents is to be carried out if possible In the case of infection of the cyst antibiotics especially penicillin, should be given the cysts are to be treated as an abscess in the same location would be treated

Prophylaxis The host of *Echinoccus* is usually the dog from whom man becomes infected Consequently contact with infested dogs is to be avoided particularly hand contact with their feces Prevention of infestation in the dog is also useful in controlling the disease Dogs should be kept from access to infected tissue and when found to be infested should be treated with anthelmintics or destroyed

Patients with severe emaciation diarrhea, or weakness should have bed rest and a high-calorie low residue diet containing supplementary vitamins In view of the bowel ulceration, diarrhea, and tendency to bleeding, abundant amounts of vitamins A, C, D, and K should be given Anemic patients should receive iron, and severe cases should get transfusions If there is severe diarrhea and ulceration of the bowel, and if the stools contain blood and pus, treatment as outlined for Ulcerative Colitis is indicated Sulfadiazine in full dosage, streptomycin, chloramphenicol, or other wide spectrum antibiotics are indicated to combat local intestinal infection In addition, the bowel should be put at rest as much as possible Abundant fluids given by mouth, or parenterally if necessary should be taken in order to maintain a daily urinary output of at least 1500 cc Mineral depletion such as loss of calcium and sodium in diarrhea, should be replaced by saline infusions, and calcium gluconate, 10 cc of a 10 per cent solution should be given intravenously

Specific treatment with either hexylresorcinol or tetrachlorethylene is effective The night before administration of either of these drugs, the bowels should be purged with magnesium sulfate, 15 gm The next morning one of the drugs should be given on an empty stomach, followed in 2 hours by 15 to 30 gm of magnesium sulfate No food should be taken for 5 hours after administration of the drug

Hexylresorcinol is given as 0 2 gm gelatin-coated pills Adults should receive 5 of these while children are given 0 1 gm per year up to age 10 If necessary, treatment may be repeatd in 3 days

If tetrachlorethylene is to be given, for several days before treatment the patient should be on a high carbohydrate high protein, low fat diet containing abundant vitamins especially the B complex Alcohol should be forbidden for several days before therapy, during it, and for several days afterward It is wise to give calcium gluconate or calcium lactate, 0 5 gm intravenously or 2 to 4 gm orally several days before therapy The evening before treatment a light meal should be taken, followed later in the evening by a saline purge with magnesium sulfate. The next morning 3 0 cc of tetrachlorethylene in a gelatine capsule should be given to adults, 0 2 cc per year of age is the dose for children The patient is kept in bed and 1 to 2 hours after administration of the drug, 15 to 30 gm of magnesium sulfate is given Following purgation a warm cleansing enema is advisable this may be followed by food intake The food should of course be low in fat content Tetrachlorethylene should not be used if there is liver or kidney damage or marked anemia and emaciation If repeat therapy is indicated it should not be given for at least

calcium diet supplemented by therapeutic doses of the vitamins of the B complex C, and K Supplemental calcium in a dose of 3 0 to 6 0 gm of calcium lactate or calcium gluconate daily for 3 to 4 days before the drug is given is also recommended Alcohol high fat content diets oils, and fats should be avoided for 3 or 4 days before therapy because they increase the possibility of the absorption of the anthelmintic

Most treatment patterns consist of having the patient enter the hos pital where the measures above are carried out On the evening before the vermifuge is to be administered a light meal is eaten and a mild to moderate cathartic given The following morning the fasting patient is given a cleansing enema followed by the vermifuge The drug stuns the parasite thus causing it to lose its attachment A brisk purge with mag nesium sulfite is then given to force out the unattached worm and remove the vermifuge Usually the purge is given an hour or two after the anthelmintic There are many anthelmintic drugs available and selec tion depends on patient circumstances cost and individual preference

The ideal anthelmintic should be harmless to the host pleasant to take inexpensive easy to administer and in all cases it should remove all parasites in a single dose Such a drug does not exist but certain chemicals have been found to be almost ideal and specific for some of the parasitic infections Frequently there are two or three agents in common use in the treatment of a specific infection Whenever possible the less toxic ones should be employed Carbon tetrachloride is so toxic that its use should be avoided Tetrachlorethylene is somewhat less toxic and is not readily absorbed from the intestine Special care must be taken in the preparation of the patient if this drug is to be used since it has serious inherent toxic properties and severe damage can result from unwise use of it

Ascariasis

For the treatment of ascariasis crystalline hexylresorcinol has become the drug of choice A single administration will remove 90 to 95 per cent of the worms To prevent burning of the oral mucosa or gastric irritation with occasionally nausea and vomiting specially coated pills or hard gelatin capsules may be procured which are resistant to chewing and disintegrate slowly They are available in 0 1 gm and 0 2 gm amounts The patient may be allowed to eat a light meal the evening before treatment but the following breakfast should be omitted A preliminary purge is not necessary The dose of hexylresorcinol is 0 1

effective It is believed that to get the worm expelled intact with its head the stool should be passed into a vessel containing water at body temperature The oleoresin of male fern, aspidium oleoresin USP, remains the most satisfactory anthelmintic for tapeworms

Before giving aspidium it is desirable that the patient have 3 days of preparation For 2 days the food should be only soft solids, on the third only liquids An evening laxative and a morning cathartic — saline, not castor oil — are to be given on the first two days, many advise a morning cleansing enema in addition to the cathartic On the evening of the third day the laxative should be repeated and aspidium oleoresin given the next morning before any food is taken, a capsule containing 4 cc is given and repeated in one hour One hour after the second dose 15 gm of magnesium or sodium sulfate dissolved in water is given, this may be repeated in one hour if watery bowel discharge has not taken place In case the head of the tapeworm has not been identified, stools should be examined after a few weeks for evidence of persisting tapeworm infestation, and if this is found, another course of treatment should be carried out

In cases in which the patient becomes ill with nausea and vomiting, and cannot carry out satisfactorily the treatment outlined above, oleoresin aspidii by duodenal tube is advised Preparation of the patient is carried out in exactly the same manner as outlined above, but in the morning of the male fern treatment a duodenal tube should be passed under fluoroscopic control The patient is then given, through the tube, one half of a mixture of oleoresin of aspidium 6 0 cc, powdered acacia, 8 0 gm, and distilled water to make 60 cc One hour later the remaining half of the mixture is given along with a saline cathartic Proportionately smaller doses are to be used for children Since the extract of male fern is quite toxic its use is contraindicated in diseases of the heart, liver, kidneys and in pregnancy Untoward symptoms of treatment may include headache, dizziness nausea visual disturbances and twitchings If toxic symptoms become severe supportive treatment with heat and parenteral fluids is indicated along with repeated enemas to hasten evacuation

Prophylaxis Tapeworm segments passed by man should be burned or otherwise destroyed Meat and fish should be cooked thoroughly, and inspection of them should be enforced as far as possible Fortunately, cold storage often kills the parasite in meat or fish and so is an additional protection With *Tenia solium*, very rarely with *T saginata*, there is evidence of possible auto infection with resultant cysticer

Hexylresorcinol is also helpful in treating enterobiasis infection and should be given in the same manner and dosage as recommended for ascariasis

Local rectal itching may be relieved by tripelennamine (Pyribenzamine) hydrochloride or diphenhydramine (Benadryl) hydrochloride, 25 to 50 mg every 4 hours by mouth Additional measures include a careful cleansing of the anus with soap and water after each defecation It is important to keep the patient s fingers away from the anus and to maintain scrupulous cleanliness of the hands and fingernails with frequent scrubbing with soap and water during the day For involvement of the appendix surgery is indicated

In epidemiology the control of the infection is difficult since studies have shown that the resistant eggs may be found in household dust from floors furniture doorway moldings and ceiling lights Thus the dust-borne as well as the finger mouth route of infection must be controlled

Simultaneous treatment should be carried out on all infected persons in a household or institution In follow up studies it has been estimated that if eggs appear in the stools in less than 37 days after treatment the drug has failed it eggs appear between 27 and 53 days after treatment the drug may have been successful but a new infection has probably occurred If eggs appear after 54 days a new infection has taken place

Trichuriasis Whipworm

With ingestion the eggs hatch and penetrate the villi of the small intestine then return to the lumen and migrate, chiefly to the cecum less often to the appendix and the colon Here they become firmly attached and are not amenable to easy eradication Whipworms are quite resistant to the more common anthelmintics After the precautions recommended to combat tetrachlorethylene toxicity in hookworm infection have been taken the following treatment is advised Early in the morning the patient should be given a tepid high saline enema, followed by 15 to 30 gm of magnesium sulfate by mouth A saline purge the night before treatment is begun may also be desirable Then on an empty stomach 2 5 cc of tetrachlorethylene combined with 0 3 cc of oil of chenopodium is given as an adult dose For children the dose is comparably smaller This should be followed after 2 hours by a second saline purge Treatment may be repeated at weekly intervals for several weeks Frequent stool examinations should be a guide for repeated treatment

CHAPTER XXV

DISEASES DUE TO NEMATODES

The treatment of infection with nematodes or roundworms is best considered under 2 headings (1) general measures applicable to all patients, and (2) the treatment of specific parasite infection

General Measures of Treatment

The nematodes vary considerably in their deleterious effects on the human body, some being relatively innocuous, others quite harmful Whether they are harmful or not their elimination from the body whenever possible is demanded for aesthetic and social reasons

For the more common nematodes to be discussed in this section the best results are obtained by eliminating the worm from the gastrointestinal tract When the parasites invade body tissue, such as the lungs, liver striated muscle, and so forth elimination may be very difficult if not impossible

Many patients are emaciated anemic and in a chronic state of ill health from long continued parasitic activity Tuberculosis, chronic skin lesions vitamin deficiencies and severe mental disturbances may complicate the treatment The general measures recommended in Part I should be instituted Anemia, when severe may require blood transfusion before specific therapy is begun Iron should also be given A highly nutritious diet supplementary vitamins sedatives to control restlessness, and antihistaminic drugs to control itching are indicated in the severe case When possible it is better to have the patient in an improved or improving physical state before the anthelmintic is given

When the more toxic drugs such as the chlorinated hydrocarbon tetrachlorethylene are to be given, a definite effort should be made to see that the liver is protected by a high protein, high carbohydrate, high

does not guarantee the absence of the parasite Proper garbage disposal in the community is important in decreasing possible rat infection

Hookworm

The results of hookworm infection of the body can be quite debilitating, proper and vigorous treatment is therefore of much more importance than simply removing a nuisance factor from the intestinal tract Therapy is quite effective but needs to be prolonged in many cases, a single treatment seldom removes all of the parasites The anemia must be treated separately in order to obtain the best results

Tetrachlorethylene has become the anthelmintic of choice because of its efficacy and relative lack of toxicity It will usually remove 80 to 90 per cent of the worms with the first trial If ascaris infection is present it should be treated before the use of tetrachlorethylene Some observers believe that diet and purgation in preparation for the treatment are not essential most observers however, favor early morning administration of the drug on an empty stomach with purgation the night before with magnesium sulfate, 15 gm in water followed by 2 glasses of water The tetrachlorethylene is administered in hard gelatin capsules, the adult dose is 3 cc and the childrens dose is 0 2 cc for each year of age Care must be taken to avoid giving cracked or damaged capsules A saline purge with magnesium sulfate 15 gm should be given 1 or 2 hours after administration of the drug Food should be withheld for several hours and alcohol in any form should be omitted from the diet for 48 hours No fats, including milk should be given for 2 days before administering tetrachlorethylene

Since a single treatment is seldom completely effective stools should be re examined in 5 to 6 days and if ova or parasites are still present, as they usually are treatment should be repeated in 7 to 10 days after the first trial

The following drugs although adequate, are either more toxic or less effective than tetrachlorethylene, but they may be employed if tetrachlorethylene is not available or cannot be used

Although oil of chenopodium will remove the worms about as effectively as tetrachlorethylene i e 70 to 90 per cent of them, excessive absorption or an idiosyncrasy has been the cause of a considerable number of deaths For adults it is administered on an empty stomach in hard gelatin capsules, 3 doses 0 5 cc each are given at half hour intervals

gm for each year up to 10 years of age For all others, the adult dose, 1 0 gm is to be given A saline purge of 15 to 30 gm of magnesium sulfate should be given 2 hours after treatment, and no food allowed for 5 hours after taking the drug The patient may be ambulatory If necessary, the treatment may be repeated after 3 or 4 days Tetrachlorethylene and carbon tetrachloride should not be used since they may stimulate the migration of viable ascarida with resultant invasion of organs outside the intestine or the appendix Surgery may be required for intestinal obstruction from masses of ascaris worms or in biliary, appendiceal, or peritoneal invasion

In the epidemiology of this infection the control lies in the prevention of dooryard pollution with feces by young children The eggs of the parasite are highly resistant and accumulate in the dirt of the playground, where they contaminate the hands

Enterobiasis

With enterobiasis or pinworm infection the oral administration of methylrosaniline chloride [gentian violet] has proved highly effective Cures in up to 90 per cent of the cases result from a course of treatment The patient may be ambulatory The drug is administerd in a dose of 60 mg as a water-soluble coated 4 hour type tablet 3 times a day before each meal for 10 days If necessary the treatment can be repeated after a 7 day rest period The recommended daily dosage for childrn is 30 mg 3 times a day for each year of age The drug is well tolerated If toxic symptoms such as nausea vomiting abdominal pain, diarrhea headache or dizziness appear the dose may be reduced or omitted for a day or two and treatment then resumed In refractory cases duodenal intubation and the instilling of 25 cc of a 1 per cent solution give good results

Leche de Higueron (Ficin) when it can be obtained, is also excellent in treating enterobiasis The patient is prepared by an evening purge with 15 to 30 gm of magnesium sulfate In the morning the fasting patient is given 60 cc of the drug with sodium bicarbonate This is followed in two hours by 15 to 30 gm of magnesium sulfate The treatment may be repeated in 1 week if necessary This sap is non-toxic and is highly destructive to the parasite The fact that it must be prepared freshly limits its usefulness since it is not readily available in most parts of the world

against the specific cause When the eruption is due to nematode larvae (*Ancylostoma braziliense, A Caninum*), the most satisfactory results are obtained by freezing the skin in the advancing area (tunnel) of the lesion Carbon dioxide snow or ethyl chloride are effective Large areas infected with parasites require ethyl acetate fumigation for relief Cover the areas with gauze soaked in ethyl acetate and wrap rubber tissue over the gauze to prevent evaporation Leave gauze in place 15 to 20 minutes Repeated fumigations at 24 hours intervals are required to kill most of the larvae The remaining parasites may be removed by freezing plus curettage Ultraviolet irradiation sufficient to produce erythema has also given cures Diethylcarbamazine (Hetrazan) by mouth in a dose of 2 to 3 mg per kilogram of body weight has also given promising results Another nematode larvae, *Gnathostoma spinigerum*, usually requires radical excision In the case of fly larvae *Gasterophilus*, the organism may be removed from its skin burrow with a sterile sharp needle, this treatment should be followed by the application of a mild antiseptic dressing

Secondary infection is often a problem and should be treated promptly by cleansing the area and applying wet dressings soaked in 1 20 solution of aluminum acetate [Burow s solution] Blisters and all infected burrows should be drained Occasionally antibiotics are indicated to manage these local infections

When severe pruritis occurs tripelennamine (Pyribenzamine) hydrochloride or diphenhydramine (Benadryl) hydrochloride 50 mg given by mouth every 4 hours may aid in relieving the itching and if the latter drug is given at bedtime it will in many cases induce sleep

Prophylaxis consists in the avoidance of skin contact with areas in which dogs and cats have defecated Some suggest a bi yearly examination of feces of pet dogs and cats for nematode ova followed by anthelmintic therapy of animals whose tests are positive

Filariasis

There are several varieties of filariasis the most important of which is that due to *Wuchereria bancrofti* The other forms are caused by *Wuchereria malayi, Dracunculus medinensis, Onchocerca volvulus*, and *Loa loa* Since there is at present no completely satisfactory specific treatment, therapy must be directed toward symptoms as well as against the location of the infection in the body in lymphatic vessels and tissues and in subcutaneous tissues

Hexylresorcinol in doses of 0 5 to 1 0 gm by mouth, preceded and followed by a saline purge as already outlined, helps in removing the worms but complete cures can seldom be secured with it

An efficient remedy, Leche de Higueron (Ficin), exists in Mexico and Central America but is too unstable to transport and market in the United States It is a proteolytic enzyme expelled by the fresh latex of certain wild fig trees Doses of 30 to 60 cc are relatively non toxic and are specific in eliminating the whipworm from the body

Trichuriasis is not infrequently the cause of acute appendicitis The appendix should be removed surgically and after adequate convalescence, further anthelmintic therapy should be carried out

Occasionally *Trichuris trichuria* occurs in association with *Ascaris lumbricoides* and *Necator americanus* As trichuriasis is the lesser evil in such symbiosis, the other infections should be given preference in treatment After their eradication with the proper anthelmintics, the trichuriasis may be attacked if it still persists

The epidemiological measures comprise chiefly personal cleanliness and prevention of contamination of food, drink, and fingers with soil containing embryonated eggs

Trichiniasis

For the acute attack of trichiniasis with its nausea vomiting, and diarrhea particularly in the first 24 hours a brisk purge should be administered such as castor oil 30 to 60 cc or magnesium sulfate, 30 gm This will augment the diarrhea and lead to expulsion of the parasites High cleansing enemas should also be given

After invasion into the blood stream organs and muscles has taken place there is no known effective specific treatment against the worm All of the anthelmintics x rays radium, the arsenicals, dyes, and even the antibiotics have been tried without success Corticotropin may aid clinical symptoms but appears not to alter the pathological physiology

For the muscle pains that follow sodium salicylate or acetylsalicylic acid in large doses, 0 6 to 1 0 gm every 4 hours while the patient is awake can be quite effective The edema particularly of the face subsides spontaneously in a few days and requires no specific therapy

The only effective prevention of the infection is the proper cooking of meat and meat products particularly pork Federal inspection of meat

doses of 0 3 gm by intramuscular or intravenous injection on alternate days for 5 to 7 weeks An alternate method is to apply it as in kala azar, beginning with 0 1 gm and on alternate days increasing to 0 2 gm, then to 0 3 gm, to a total of 3 0 gm In children the initial dose is 50 mg and the maximum dose is 0 2 gm

Another new compound that reduces the microfilaria in the blood and has produced excellent results in filariasis is diethylcarbamazine (Hetrazan) In the average case 2 0 to 4 0 mg per kilogram of body weight is given orally 3 times a day and should be continued for at least 3 weeks A smaller dose of 0 2 to 0 5 mg per kilogram of body weight daily is advised however for patients who react sharply to treatment or who have a severe filarial attack with sensitization to filarial protein Doses as large as 12 to 20 mg per kilogram of body weight daily may be tolerated The optimum duration of treatment can only be estimated on the basis of reactions maximum treatment should be continued for at least 3 weeks after the disappearance of the last systemic reaction

Systemic reactions to diethylcarbamazine (Hetrazan) are usually mild and of short duration and include headache drowsiness nausea and malaise It may cause nodular swellings lymphangitis abdominal pain and exaggeration of existing swellings all thought to be due to filarial protein These call for continued treatment until long after they have subsided

For secondary infection with streptococci or staphylococci sulfadiazine or penicillin or both should be used Neither of these chemotherapeutic agents has any appreciable effect on the filariasis per se If organisms other than streptococci or staphylococci have become secondary invaders the appropriate antibiotic should be chosen for the organism that has been recovered

For ulcers on an elephantoid leg local application of a 3 per cent ointment of aureomycin or aureomycin powder plus tight strapping of the whole affected part for several days is helpful Such serious conditions as epididymo-orchitis and funiculitis can be treated very effectively with sulfadiazine or penicillin as already outlined

A vaccine consisting of 10 million hemolytic streptococci of many strains and 50 million staphylococci of several strains of aureus and albus has been used by Roa at the Calcutta School of Tropical Medicine for 15 years in more than 50 000 cases with good results It is given intracutaneously in doses of 0 02 to 0 1 cc twice weekly to a total of

in the morning Children may be given a dose of 0 03 cc per year up to 15 years of age Although oil of chenopodium is used in the treatment of ascarides when ascaris is present along with hookworm, preliminary treatment of the ascaris with hexylresorcinol is preferred

Hexylresorcinol though relatively non toxic, is much less effective than chenopodium removing only 50 to 60 per cent of hookworms with one treatment The dose for an adult is 1 0 gm prepared in hard gelatin capsules and given on an empty stomach For children the dose is 0 1 gm for each year up to the age of 10 When ascaris is also present, hexyl resorcinol is the drug of choice and should be used to remove the ascarides before the treatment for hookworm is undertaken

Thymol is used preferably in capsules and is mixed with equal parts of powdered lactose or sucrose 1 0 gm is given on an empty stomach every hour for 4 hours Some prefer using the total dose of 4 0 gm in a single administration For children the dose is 0 3 gm per year up to the age of 15

Carbon tetrachloride although effective against hookworm, should not be used because of its severe toxicity

Although hookworms do not infect the appendix symptoms suggesting appendicitis especially in children are not uncommon, particularly in an endemic area If a normal temperature lack of rebound pain slight or no leukocytosis with an eosinophilia anemia and ova in the stools are present and if hookworm disease is the cause of these symptoms, operation for acute appendicitis should be avoided

The anemia of hookworm infection is of the simple, hypochromic, microcytic variety Ridding the body of the parasites gives rise to some improvement in the blood condition but does not cure the anemia Likewise large doses of iron will usually cause a rise in hemoglobin and red blood cell level even though the parasites are still present in the body, but this beneficial effect tends to be transient The best, and most permanent results in the blood picture are to be obtained by the elimination of the worms from the body, followed by large doses of iron such as ferrous sulfate or ferrous gluconate, 0 3 to 0 6 gm 3 times a day, until the blood is normal An improved abundant diet, rich in vitamins should supplement this treatment

Creeping Eruption

Since various types of larvae can cause a dermatitis for which the generic term is creeping eruption, the treatment should be directed

species carried out As with malaria, personal measures include adequate housing screening of doors and windows the use of bed nets and the adequate application of Chlorophenothane [DDT]

Dracontiasis When *Dracunculus medinensis* (dragon worm Medina worm, Guinea worm dracunculosis) is the cause of the filariasis, the supportive measures outlined above should be carried out, with bed rest and immobilization of the affected part Local pain and itching may be controlled by the subcutaneous administration of 0 5 cc of 1 1000 epinephrine hydrochloride or by the oral administration of antihistaminics

When the worm first makes its appearance it should not be disturbed as after parturition it may leave spontaneously When the worm begins to protrude from the skin it may then be rolled on a small stick and a thread tied around it to prevent retraction Gentle traction may be applied to the worm each day to aid in its expulsion The stick should be attached to the skin with adhesive tape and a sterile dressing applied Great care should be exercised in this extraction in order to prevent tearing of the worm as this may be followed by severe inflammation Frequent cold water douching of the ulcer at the skin opening and of the part occupied by the worm may hasten the complete expulsion of the larvae after which the worm may emerge spontaneously or may be extracted gently without resistance

A hot emulsion containing 2 0 gm of finely powdered phenothiazine 0 3 gm lanolin and 5 0 cc of sterile water in 35 cc of sterile olive oil may be injected into the vicinity of the worm relaxing it for easier removal This kills the worm usually in about 7 days If the worm is visible it may then be extracted

Control measures consist in the proper boiling of all drinking water and possibly the placing of small fish in bodies of fresh water that contain the cyclops

Onchocerciasis

This disease caused by *Onchocerca volvulus*, commonly produces tumerous swelling in the skin overlying bony prominences The usual treatment is simple surgical removal of accessible swellings Treatment with suramin sodium (Naphuride) U S P as recommended for African Trypanosomiasis and diethylcarbamazine (Hetrazan) as recommended for filariasis show encouraging results These agents may cause unpleasant reactions however such as pruritus fever and progression of ocular reactions in many cases Hetrazan apparently causes

Filariasis due to *W bancrofti* is the most serious of the infections named above The Malaya form is similar, though usually much milder, since both involve lymphatic structures their treatment will be considered together

In the early infective state in addition to constitutional symptoms, there may be allergic manifestations For these epinephrine hydrochloride 0 5 cc of *1 1000 solution* may be used subcutaneously The antihistaminics such as diphenhydramine (Benadryl) hydrochloride or tripelennamine (Pyribenzamine) hydrochloride, in doses of 50 mg 3 or 4 times a day may be tried

For the constitutional symptoms bed rest is imperative as activity aggravates or may precipitate the inflammatory process The affected part should be elevated to assist drainage On an extremity a moderately firm bandage may be applied to prevent swelling, for the genitals and scrotum a suspensory bandage should be used Codeine sulfate, 30 mg hypodermically is usually effective for pain, if pain is severe, morphine sulfate 8 mg may be necessary Compresses either hot or cold should be applied over local inflamed areas During the acute manifestations all local surgical operations are considered undesirable except as emergency measures

Various antimony compounds have been tried with varying success, perhaps the best results having been obtained with lithium antimony thiomalate (Anthiomaline) Given intramuscularly in doses of 2 0 to 4 0 cc of a 6 per cent solution every other day for 10 doses, it is thought to be effective in reducing the microfilarial count in the blood It may cause toxic symptoms however such as fever joint pains, vomiting, and sometimes skin rashes

Sodium arsanilate (Soamin) appears to be quite satisfactory in controlling symptoms in the early stages It has little effect on the microfilarial count, but it reduces fever and lymphangitis It may be given subcutaneously intramuscularly or intravenously in doses of 0 02 to 0 2 gm increased to 0 3 to 0 5 gm, dissolved in distilled water and given every other day Usually it is non toxic Tryparsamide in doses of 2 0 to 3 0 gm intravenously 2 or 3 times a week is considered by some to be useful in controlling the symptoms of chyluria Such compounds as antimonyl tartrate or stibophen (Fuadin) are not particularly effective Other antimony compounds such as stibamine glucoside (Neostam) and urea stibamine do give some cures Of this group diethylammonium p-stibanilate (Neostibosan) has been used rather widely, it is given in

The examination of duodenal contents for ova and parasites is coming to be considered a more reliable index of persistence of infection with this parasite than simple stool examination, hence there has been an increasing popularity of the use of duodenal installations in the treatment of this condition

So called hyperinfection may be avoided by properly combatting constipation during treatment

Since strongyloidiasis is acquired chiefly by penetration of the skin by the ova the epidemiological measures against it consist primarily of not walking barefoot or otherwise exposing the skin to polluted soil Prevention consists further of the proper disposal of human excreta and the adequate treatment of detected cases

Loiasis

This disease, caused by the parasite *Loa loa* and spread by the *Chrysops dimidiatus*, is characterized by fugitive swellings, also called Calabar swellings because of the prevalence of the disease in that part of Africa. These swellings behave as though they were allergic like responses to the discharges of microfilariae Urticaria and frequently irritative lesions of the eye occur Swellings should be treated by ice packs, and the itching and urticaria are helped by the injection of 0 3 to 0 5 cc of epinephrine hydrochloride, 1 1000 subcutaneously Antihistaminics such as diphenhydramine (Benadryl) hydrochloride or tripelennamine (Pyribenzamine) hydrochloride 50 to 100 mg by mouth 3 or 4 times a day, may also be helpful When pain is severe acetylsalicylic acid, 0 6 gm every 3 hours by mouth, or codeine phosphate, 30 mg orally every 6 hours, will usually give satisfactory relief If these drugs do not give relief of pain methadone, 5 to 10 mg intramuscularly, or morphine sulfate 8 mg subcutaneously should be given

If the worm is seen in sites such as the conjunctiva it should be cut down upon and extracted

Diethylcarbamazine (Hetrazan) in a dose of 2 0 mg per kilogram of body weight 3 times a day for 3 weeks is effective and promptly clears the microfilariae from the blood stream and cures the infection For the first few days of treatment with this drug the patient should be under close observation since some individuals develop reactions probably owing to the rapid destruction of the parasites

15 to 20 injections It is claimed to have ameliorative effects in the absence of secondary infection

From studies carried out on military personnel who had acquired filariasis in the South Pacific islands it became apparent that one of the most important measures of treatment was the removal of the patient to a climate where the disease did not exist, in this case to the United States Sometimes that was all the treatment required, for spontaneous recovery occurred frequently A second significant feature of that experience was the importance of proper psychotherapy giving full assurance that the genital involvement in the male did not lead to transmission of the infection and, more important, to impotence

Elephantiasis also called elephantoid fever, is usually the result of repeated infection with filariae During the acute symptoms bed rest, a liquid diet free purgation and sedatives to painful areas are necessary, just as in the acute form For the chronically swollen extremity, most commonly a leg and the genitals careful plastic surgery, such as the Kondoleon operation or modification thereof, for the removal of strips of subcutaneous tissue may be attempted

The Auchincloss operation accomplishes this In this procedure two parallel skin incisions joined at each end by a V-shaped incision are made in the long diameter of the limb a wedge shaped piece of skin and blubbery tissue is removed with painful spots included if possible, the skin is under cut on each side then drawn together and the wound closed Amputation is seldom if ever a justifiable procedure

Large scrotal swelling and elephantiasis of the mamma or vulva may be removed with great relief to the patient In chronic swellings however nothing short of complete removal should be attempted For lesser degrees of lymphedema an elastic stocking such as that used for the usual phlegmasia alba dolens may be sufficient for comfort and may prevent further increase in the swelling According to some, better results are obtained, even at this stage by bandaging the limb tightly than by surgery

The treatment for chyluria is complete rest the elimination of all fat from the diet and the use of mild saline catharsis Clots in the bladder may have to be washed out with warm boric solution or with 1 2000 solution of silver nitrate which also has some styptic action

The epidemiological measures against *Wuchereria filariasis* consist of adequate mosquito control Proper identification should be made of the mosquito vector, whether it is *Culex quinquefasciatus*, *Aedes scutellaris*, or *Anopheles annctus*, and the most effective attack against the given

PART VIII

DISEASES OF UNDETERMINED ETIOLOGY

CHAPTER XXVI

MISCELLANEOUS DISEASES OF UNDETERMINED CAUSE

Epidemic or Infectious Pleurodynia Bornholm Disease Epidemic Myalgia

With few exceptions this disease is of short duration fever pain in the lower thorax often on only one side and pain in the back are the chief symptoms So far no specific therapy has been developed, and the etiological agent remains undiscovered, although recent evidence strongly indicates that it is caused by the Coxsackie viruses Simple symptomatic treatment is advised this is concerned chiefly with the pain A recumbent position is usually the most comfortable Strapping the lower ribs with adhesive tape or the use of a chest swathe often helps Prompt use of acetylsalicylic acid in doses of 0 2 to 0 3 gm every 2 or 3 hours usually suffices With continuing more severe pain methadone hydrochloride 5 to 10 mg or meperdine (Demerol) hydrochloride 50 to 100 mg should be given and repeated as needed for relief Sulfonamides penicillin and other antibiotics have been tried but are not effective

Prevention Since the disease spreads rapidly in its epidemic form person to person contact seems the probable source of dissemination Consequently isolation of the patient seems advisable even though there has been very little evidence of control from this procedure At present there is no other preventive measure to advise

more reactions and its effect is not as lasting as that of Naphuride Plasmochin in a 0 1 per cent solution may be injected into the anterior chamber of the eye in an attempt to arrest ocular involvement

Prophylaxis consists of wearing sufficient clothing to protect the skin from bites of the vector fly Chlorophenothane [DDT] in pools and streams kills the larvae

Strongyloidiasis

Strongyloides stercoralis sometimes involves more tissues of the body than simply the gastro intestinal tract, a fact too frequently overlooked in the treatment of this infection

Methylrosaniline chloride U S P [gentian violet] has been found to be the most effective treatment When the parasite is confined to the intestinal tract as it usually is 60 mg in 30 mg enteric coated capsules 3 times a day before meals for 16 days, is recommended For children, 10 mg for each year of apparent age should be given daily for a period of 2 weeks Oral administration cures 90 per cent of these cases killing the adult worms more readily than the larvae or eggs Satisfactory results with such dosage have been reported after only 7 to 10 days instead of the usual 16 days Somewhat better results are obtained from the use of gentian violet by stomach or duodenal tube, giving slowly 25 cc of a 1 0 per cent solution and leaving the tube in place for an hour The intubation method is advised if the simple oral method fails

If toxic symptoms occur such as nausea, vomiting, abdominal pain, diarrhea, headache, and dizziness the dosage should be reduced or omitted for a day or two and then treatment may be safely resumed Alcohol must be avoided during treatment

If the patient shows evidence of severe infection, hyperinfection, or infection outside the intestinal tract, intravenous gentian violet is indicated For this purpose a 0 5 per cent solution is used, 25 cc given slowly on alternate days for 4 to 15 doses This is advised particularly for pulmonary infections

Some have advocated the use of tincture of iodine by duodenal tube for effective elimination of strongyloides The patient should be given a saline purge an hour before the evening meal, and no breakfast the next morning Compound solution of iodine [Lugol s solution], 4 0 cc, is then introduced into the duodenum on alternate days until neither the feces nor the duodenal washings show any ova or parasites

PART VIII

DISEASES OF UNDETERMINED ETIOLOGY

CHAPTER XXVI

MISCELLANEOUS DISEASES OF UNDETERMINED CAUSE

Epidemic or Infectious Pleurodynia Bornholm Disease Epidemic Myalgia

With few exceptions this disease is of sho t duration fever pain in the lower thorax, often on only one side and pain in the back are the chief symptoms So far no specific therapy has been developed and the etiological agent remains undiscovered although recent evidence strongly indicates that it is caused by the Coxsackie viruses Simple symptomatic treatment is advised this is concerned chiefly with the pain A recumbent position is usually the most comfortable Strapping the lower ribs with adhesive tape or the use of a chest swathe often helps Prompt use of acetylsalicylic acid in doses of 0 2 to 0 3 gm every 2 or 3 hours usually suffices With continuing more severe pain methadone hydrochloride 5 to 10 mg or meperdine (Demerol) hydrochloride 50 to 100 mg, should be given and repeated as needed for relief Sulfonamides, penicillin, and other antibiotics have been tried but are not effective

Prevention Since the disease spreads rapidly in its epidemic form person to person contact seems the probable source of dissemination Consequently isolation of the patient seems advisable even though there has been very little evidence of control from this procedure At present there is no other preventive measure to advise

BIBLIOGRAPHY

Diseases Due to Nematodes

1 AUGUSTINE D L Diseases Due to Nematodes or Roundworms" *Oxford Medicine* 1948 v p 9-1
2 BLAIR D LOVERIDGE F MEESER C and ROSS W Urinary Schistosomiasis Treated with Miracel D *Lancet*, 1949, i p 344
3 BURCH T A Experimental Therapy of Onchocerciasis with Suramin and Hetrazan *Bol Ofic San Panam* 1949 xxviii p 233
4. CULBERTSON J T Experimental Chemotherapy of Filariasis," *Jr Roy Soc Trop Med and Hyg*, 1947, xli, p 18
5 HAWKING F and LAURIE, W Action of Hetrazan on Filariasis and Onchocerciasis *Lancet* 1949 ii p 146
6 KIRBY-SMITH J S The Treatment of Creeping Eruption, *South Med Jour* 1935 xxviii p 999
7 LUONGO M A REID D H and WEISS W W Effect of ACTH on Trichina, *N E J Med* 1951 ccxlv p 757
8 MURGATROYD F and WOODRUFF A Loiasis Treated with Hetrazan (Banocide) *Lancet* 1949 ii p 147
9 SHATTUCK C G *Diseases of the Tropics*, Appleton Century Crofts Inc. N Y 1951, p 554.

units each 24 hours If a focus of tuberculous infection is found, streptomycin or dihydrostreptomycin should be given as outlined for Tuberculosis The *coccidioides immitis* (coccidioidomycosis) is a frequent cause of erythema nodosum in various parts of the United States and when it is the cause the skin lesions usually heal spontaneously Neither penicillin nor streptomycin has any effect on them

If acute rheumatic fever which is often the cause of erythema nodosum is present the patient should be treated as outlined in the section on Rheumatic Fever

For comfort the patient may be given sodium salicylate 1 0 gm every 4 or 6 hours together with comparable doses of sodium bicarbonate or acetylsalicylic acid 0 6 to 1 0 gm every 4 hours

Local irritation may be relieved by the application of weak sodium bicarbonate solution boric acid solution or weak alcohol A dusting powder may be applied Calamine lotion may be similarly used The lesions usually subside in 3 to 6 weeks but frequently they recur

Exanthema Subitum Roseola Infantum

This is an acute infectious disease of brief duration No special treatment beyond bed rest seems indicated The disease is of unknown etiology and no specific therapy has been developed As a leucopenia is present it seems advisable to avoid any drugs likely to decrease the number of polynuclear leucocytes If the leucocytes fall below 2000, penicillin or one of the broader spectrum antibiotics may be given to prevent possible bacterial invasion

Relapsing Febrile Non Suppurative Panniculitis

This form of panniculitis is another disease of unknown etiology for which there is no effective specific remedy Sulfonamides penicillin, and other antibiotics as well as many other therapeutic agents have been used but slight if any, benefit has resulted from them A recurring disease with prolonged periods of fever it is almost ideal for clinical trial of antibiotics or other remedies its relative rarity may explain why an effective therapy has not been found in this way

General measures as described in Chapter 1 including bed rest and an ample nutritious diet should be applied as indicated by the patient s

Miliary Fever

There is no known treatment for this disease Therapy is entirely symptomatic Complete recovery is the rule

Febricula

Fevers of unknown etiology, although usually mild and self-limiting, are shortened and the patient made more comfortable by bed rest, increased fluid intake, and employment of the general measures outlined in Part I

Penicillin aureomycin, chloramphenicol, terramycin, streptomycin, or dihydrostreptomycin may be given therapeutic trials, since many of the fevers of short duration may be bacterial infections that will respond to one or the other of these drugs These measures are designed to prevent a febrile disease that is not immediately diagnosable and is consequently called febricula With improved methods of early diagnosis these situations become less and less frequent

A careful check of serum titers 2 to 12 weeks after the illness may reveal the true identity of the fever

Erythema Nodosum

The patient with erythema nodosum can be quite ill, although painful lesions of the legs are usually the only symptoms The patient should be confined to bed and should receive food high in calories and vitamins sufficient fluids to insure a daily urine output of 1500 cc, and adequate nursing care A simple cradle without heat may be used to protect the extremities from the bed clothing

Since this disease is generally considered to be a tissue manifestation of bacterial allergy including tubercle bacilli and streptococci, diligent search should be carried out for any foci of infection, and if susceptible organisms are found treatment with the appropriate chemotherapeutic agent should be instituted This refers principally to the use of penicillin in streptococcal infections, streptomycin or dihydrostreptomycin in tuberculosis Depending upon the susceptibility of the organisms found penicillin may be given either in aqueous solution, 30,000 to 40 000 units every 4 hours, or in the form of the longer acting preparation, 300,000

receive 100 to 400 mg of cortisone by mouth or intramuscularly or 40 to 160 mg of corticotropin intramuscularly administered daily in 4 divided doses After satisfactory response a daily maintenance dose of 100 to 150 mg of cortisone or 50 to 100 mg of corticotropin is advised Treatment with these substances is still in the experimental stage and many careful studies are needed before the therapeutic value and the best dose procedures can be stated authoritatively Rest periods are necessary because of the development of untoward reactions Frequently these are so severe as to prohibit the use of the drugs

The skin eruptions usually do not need any local treatment Occasionally a severe, distressing burning sensation is noticed Relief from this may be obtained by the oral use of one of the antihistaminic drugs such as diphenhydramine (Benadryl) hydrochloride given in a dose of 50 mg every 4 hours Tripelennamine (Pyribenzamine) hydrochloride may be substituted for diphenhydramine if toxic side reactions to the latter develop, a dose of 50 to 100 mg 2 to 4 times a day is usually satisfactory Local applications of a 2 per cent boric acid solution may also be helpful Sedatives such as chloral hydrate 0 5 to 1 0 gm given once daily or phenobarbital 30 mg 2 or 3 times a day, are advised if there is much restlessness or if the skin irritation is causing distress Joint pains respond poorly to the salicylates and may require methadone 5 to 10 mg every 4 hours for relief

Quinine sulfate may prove beneficial in certain cases At times it produces a remission in a case that has smouldered for many weeks without any indication of improving It is wise to start with a small dose and gradually to increase the amount taking care to avoid toxic reactions A satisfactory initial dose is 0 6 gm by mouth 3 times a day This is increased until the patient is taking 1 8 gm 3 times a day If dizziness or tinnitus appears the dose should be reduced so that it may be continued for weeks or months without any distress

Bismuth also is useful in treatment but should be avoided in the active phase Care must be exercised when it is used to avoid activation of a latent subacute state Bismuth should be given intramuscularly a soluble form in which the dose and length of action can be controlled more accurately is recommended The drug must be discontinued at once if there is any indication of reactivation Careful check must be made of the urine and blood to detect any reactivation as early as possible Sodium bismuth tartrate 30 mg 2 or 3 times a week for 8 weeks is effective Bismuth salicylate may also be used in a dose of 0 1 gm given once a week

condition, for as long as fever persists Fortunately, discomfort from the local subcutaneous lesions is only moderate, and rarely do they break down and discharge material from necrotizing lesions Infection of them is very rare Consequently, local treatments, beyond a sterile dressing if breakdown does occur are not needed

As there has been no evidence that this disease is communicable, isolation precautions seem unnecessary

Lupus Erythematosis

Choice of therapy for this malady must be guided by the type of lesions exhibited and by the phase of the disease Acute and subacute disseminated lupus erythematosis has been resistant to all known therapeutic procedures, and treatment is often discouraging In this phase great care must be taken to see that the therapeutic procedures employed do not harm the patient Bed rest is essential and must be as complete as possible The patient should be in a quiet, darkened room, direct sunlight must be excluded, and the patient must not be exposed to ultraviolet light at any time A high calorie high-vitamin diet made as palatable as possible in accordance with the patients dietary habits and special preferences, should be started at once Every effort must be made to counteract anorexia and to secure a high calorie intake If severe anemia is present blood transfusions should be given Local painful areas are helped by hot applications If there is acute inflammation of the mouth, frequent gargling and rinsing of the mouth with the alkaline mouthwash—N F [Dobell s solution] are recommended In these cases care must be taken also to avoid further injury to the mucous membranes by selecting food that is non irritating A soft diet, taken only when the food is not too hot is usually satisfactory

At present much attention is being given to the treatment of lupus erythematosis with corticotropin and cortisone with conflicting reports in regard to the best dosage and the results Some claim cure, most claim amelioration, some claim absence of any real effectiveness, all report undesirable, often severe and sometimes fatal side results Relapse seems to be the rule following treatment with corticotropin and cortisone The best results with steroid hormones appear to occur in early cases In a disease such as this which as a rule is eventually and sometimes speedily, fatal, trial with these treatments in the hands of those experienced in their application seems justifiable Patients to be treated should

Fourth Disease

There is no known treatment for this scarletiniform exanthem known as the fourth disease Isolation of the patient until the eruption fades is about all that is necessary

Onyalai

In the treatment of this hemorrhagic disease which is a form of thrombocytopenic purpura occurring in Africa ascorbic acid in large dosage totaling 2 to 8 gm in 7 days has proved effective For patients unable to take ascorbic acid by mouth sodium ascorbate in a daily dose of 0 1 to 0 gm or more for adults and 30 to 50 mg for infants may be given intravenously If synthetic ascorbic acid is not available sterile lemon juice 10 to 15 cc with equal amounts of normal saline given intravenously 2 or 3 times a day will yield the same therapeutic results Corticotropin 40 to 80 units intramuscularly or cortisone 300 mg by mouth daily, may be helpful They should be given in these amounts for a few days and then the respective dose of each should be reduced to one half

Prophylaxis depends on an adequate diet rich in ascorbic acid or on the giving of ascorbic acid as directed in the section on Deficiency Diseases

Big Heel Epidemic Enlargement of Os Calcis

This is a tropical disease known to occur in Africa and Formosa Of unknown etiology it develops in the wet season After a few weeks recession of bone enlargement begins and is usually complete in about 4 months So far no specific treatment has been developed Protection from the wet may be of value in prophylaxis Prevention of trauma to the foot and rest seem of use in expediting recovery

Barcoo Sickness

Treatment of this disease is mainly supportive Aluminum hydroxide magnesium trisilicate gel (Gelusil) in 15 cc doses every hour or two

In the acute and subacute disseminated forms in females successful remissions may occasionally follow temporary sterilization by x ray or the suppression of female sex hormones by administration of male sex hormones Testosterone propionate, 10 to 25 mg intramuscularly 3 times a week, may be given until a good result is seen or until signs of change in sex characteristics appear, such as voice or hair growth changes Small doses of x-ray in the order of 25R daily for 3 to 6 days, repeated for 3 courses, may help certain cases by its effect in modifying antibody response

Some success has been obtained also from para aminobenzoic acid When applied as a 5 per cent ointment, it is effective in blocking ultra violet light, in some patients good results are obtained also by oral administration in an initial dose of 2 to 4 gm followed by a 1 gm dose every 2 hours This follow-up dose should be increased or decreased depending on the patient s response or signs of toxicity

Patients in remission should be careful to avoid direct exposure to sunlight Protection by clothing glass ultraviolet absorbent ointments, or lotions is helpful activities should be regulated as far as possible to avoid ultraviolet light

Chronic localized skin lesions may respond to gold therapy in the form of gold sodium thiosulfate in a weekly dose of 10 to 50 mg given intravenously for 20 weeks The larger dose is given as soon as it is evident that the patient can tolerate the 10 mg dose Local applications of Abramowitz sulfurated lotion may also be helpful in removing the skin lesion

Rx		
	Solution of sulfurated lime (N F) filtered	30 00
	Saturated solution of zinc sulfate filtered	20 0
	Glycerin	5 0

Sig Apply to spots once daily

Resistant lesions should be referred to the dermatologist for careful dermatological therapy

The sulfonamides, penicillin and other antibiotics have proved disappointing in the treatment of this disease and little is to be gained from their use Sulfonamides especially should be avoided

Prophylaxis Great care must be taken to avoid surgical procedures, vaccine therapy, sunburn exposure to cold and excessive heat

During convalescence hot baths, baking massage and exercises hasten recovery and tend to prevent disability

INOPERABLE CARCINOMA

Patients with malignant neoplasms too widely disseminated for surgical extirpation present a special problem in therapy The technique of management is such as to warrant a special description of the available means and the most efficacious methods of employing them in order that the best results may be secured

Treatment of these patients may be divided into symptomatic measures and special therapeutic agents and techniques

Symptomatic Measures Of first importance is the patient s mental reaction to his disease Since prognosis is hopeless this presents a major problem Some patients demand and want a frank discussion others prefer to remain uninformed while still others desire only a limited discussion of their illness The physician must use great tact in handling this question. He must evaluate the mental status and probable reaction of his patient to the information In general it is wise to have a frank discussion about the nature of the disease and the general course while at the same time maintaining a guarded optimism about the ultimate outcome It is essential that the physician do all that he can to instill courage, confidence mental equanimity and peace of mind These patients above all others need physicians and nurses with strong sympathetic but always hopeful personalities and ones upon whom they feel they can depend and draw strength for their ordeal A few moments spent by the physician in discussing some mental problem that is causing the patient serious distress is often far more effective in relieving pain than a powerful analgesic Above all else these patients need peace of mind Whether a patient is or is not told of the neoplasm in most circumstances it is wise to inform some responsible person close to the patient, preferably the next of kin of the true nature of the illness

Next in importance and usually closely associated with the psychological aspect of this disease is the problem of sedation and analgesics When used wisely these agents can do much to improve the mental and physical status of the patient. If advised or used unwisely they can and often do prove to be a serious handicap to the patient comfort and well being

may prove useful in controlling the nausea and vomiting Quinine sulfate, 0 3 to 0 6 gm 2 or 3 times a day, usually proves helpful

Reiter's Disease

Whether conjunctivitis urethritis and arthritis, the three manifestations of Reiter s disease are present together or separately, the patient should be confined to bed Although the infectiousness from person to person is not definitely established, precautions as outlined in Part 1 should be carried out The patient should be given a nutritious diet, high in vitamin content, with liquids forced to maintain fluid balance as well as for urethral irrigation

For the conjunctivitis saline irrigations or the use of warm boric solution may be helpful If there is corneal involvement, the help of an ophthalmologist should be sought Every attempt should be made to prevent secondary infection

For the joint pains sodium salicylate or acetylsalicylic acid in doses of 0 6 to 1 0 gm every 4 to 6 hours may be tried, but the results with such therapy often are not striking

No local treatment for the urethritis needs to be instituted The disease tends to be self-limiting but relapses are common, occurring in about 30 per cent of cases

Many types of systemic therapy have been tried for the treatment of Reiter s disease, the arsenicals mild mercurous chloride, fever therapy, and the gold salts have been found to be of little or no benefit The sulfonamides and penicillin are also ineffective A combination of penicillin and fever therapy has been tried with some success

Streptomycin has been tried with promising results A dose of either 4 0 gm in divided doses daily for 7 days or 2 0 gm a day for 10 days is recommended

Corticotropin and cortisone exert a remarkable healing effect on Reiter s disease They shorten the course and may bring about complete recovery Corticotropin 25 mg intramuscularly at 6 hour intervals for 10 to 12 days or cortisone 300 mg daily intramuscularly divided into . doses for 3 days followed by 200 mg daily for 10 days may be given If necessary 150 mg daily can be given for an additional 10 days Oral cortisone is also effective and may be given in the same dose as recommended for intramuscular injections

These agents are synergistic and exert a more powerful analgesic effect while at the same time a small dose of each of the drugs is required There are many proprietary preparations of this variety of which the following are good examples

(Empirin Compound)	Acetylsalicylic acid	0 227 gm
	Acetophenetidin	0 162 gm
	Caffeine	0 032 gm
(*Edrisal*)	Acetylsalicylic acid	0 *1600 gm*
	Acetophenetidin	0 1600 gm
	Amphetamine sulfate	0 0025 gm

They are given in doses of 1 to 2 tablets every 3 hours when necessary The caffeine and amphetamine serve as central nervous system stimulants and tend to create a temporary mild euphoria which may prove a helpful psychological effect for the patient in pain

When these preparations are no longer effective or the dosage has been increased so that unfavorable toxic effects are appearing they can be combined with sedation or with the more powerful narcotic analgesics

Usually a combination of these preparations with codeine and the judicious use of sedation should be next in order of treatment For this purpose Empirin compound with codeine and Edrisal with codeine are available The codeine content is 32 mg and generally this dosage is satisfactory, as the intensity of the pain increases an additional , mg of codeine phosphate should be given with each do e of the analgesic This combination should be continued as long as possible but when it no longer suffices the more potent and also more toxic analgesics must be started Meperidine (Demerol) hydrochloride 50 to 150 mg doses orally or intramuscularly may be given a trial It exerts an excellent analgesic effect but frequently causes nausea vomiting and serious vertigo Fortunately it does not tend to constipate the patient Methadone hydrochloride in 5 to 10 mg doses by mouth or subcutaneously may also be given a trial at this stage It too is a very potent analgesic but tends to produce nausea vomiting and vertigo Unfortunately tolerance to the analgesic effect develops all too rapidly to these drugs and increase in dosage products the undesirable side effect Many prefer to give methyl dihydromorphinone (Metopon) hydrochloride at this stage It is given in doses of 3 to 9 mg at 6 to 9 hour intervals or as required by the patient to control his pain It is a long acting powerful analgesic is effective by mouth and has much less in the way of annoying side

In general, sedation should be used sparingly It leads to mental and physical lethargy, constipation, indigestion, and mental depression When there is abnormal mental tension serious emotional unbalance, and insomnia of such a degree as to cause the patient considerable distress however, sedation is indicated There are many good sedatives and any of those recommended under General Measures in Chapter I are satisfactory The barbiturates are conveniently administered and are usually satisfactory Older patients and especially those with moderate degrees of arteriosclerosis may not respond well to the barbiturates which not infrequently cause mental confusion in such patients In these cases, chloral hydrate in doses of 0 5 to 1 0 gm may be given A convenient prescription is as follows

Chloral hydrate	10 gm
Syrup	50 cc
Water, to make	100 cc

Sig One or two teaspoonfuls in fruit juice at bedtime

Chloral hydrate however should be avoided if there is stomach irritation since it is capable of causing mild gastric irritation and may make any indigestion worse Chloral hydrate can be given satisfactorily by rectum if the oral route cannot be used A dose of 1 0 to 2 0 gm dissolved in 50 cc of saline gives excellent results

It must be kept firmly in mind that sedation should never be used alone to control pain Sedatives have limited or no analgesic effect and in the presence of pain may lead to serious untoward reactions, such as excitement and delerium When combined with an analgesic, they usually give a synergistic or additive effect which results in better control of distress than analgesics alone

Pain should be adequately controlled with those agents that give as little in the way of deliterious side effects as possible The salicylates in the form of acetylsalicylic acid 0 3 to 0 6 gm doses should be used as needed in the beginning and continued until they no longer control the pain or until the dosage has reached sufficient proportions to give undesirable or toxic side effects Gastric irritation from the salicylates can be lessened by the use of sodium bicarbonate with the drug or by using enteric-coated acetylsalicylic acid There is also available a chemically buffered proprietary acetylsalicylic acid preparation (Bufferin), which is satisfactory for use in the presence of gastric irritation

When the salicylates alone no longer give satisfactory results, they should be combined with acetophenetidin and caffeine or amphetamine

The development of tolerance leads to increased dosage and consequently to more of the undesirable effects of the drug Metopon is useful in this respect since tolerance to it develops slowly and is lost more *readily than to other morphine derivatives* It may be *alternated with* methadone meperidine or methorphinan with satisfactory results and adequate control of the tolerance factor for long periods of time

The diet should be highly nutritious and rich in *vitamins* Every effort should be made to make it palatable so that the patient will take it in sufficient quantities to maintain an adequate nutrition In the presence of anorexia, nausea or vomiting there is frequently great difficulty in maintaining an adequate food intake In the presence of hypercalcemia from osseous metastases it is frequently necessary to reduce calcium intake to 200 mg a day and force fluids to 3000 or 4000 cc a day in order to prevent renal stones and other undesirable effects Serious hypercalcemia may require intravenous infusions of 2 5 per cent sodium citrate saline and 10 per cent glucose The retention of sodium by a patient on steroid therapy requires a diet low in sodium content *Usually* a diet containing not more than 0 5 gm of sodium a day is satisfactory in controlling the edema resulting from the increased sodium retention *of hormone therapy*

An adequate iron intake must be maintained especially in patients chronically losing blood or exhibiting a secondary anemia Usually ferrous gluconate 0 3 gm 2 or 3 times a day after meals is satisfactory

Pruritus which may be a serious problem is ameliorated by diphenhydramine (Benadryl) hydrochloride 25 to 50 mg 4 times a day The analgesic drug acetophenetidin in a dose of 0 3 gm repeated if needed 3 or 4 times a day is also helpful and in combination with diphenhydramine may give relief from pruritus for long periods of time It is important to remember that morphine and its derivatives are likely to increase pruritus and consequently methadone or meperidine or the non narcotic analgesics are usually more satisfactory in the management of these patients

Infections *involving various areas* but especially the respiratory and genito-urinary tracts should be adequately controlled The newer sulfonamides sulfisoxazole (Gantrisin) or sulfadimetine (Elkosin), are excellent for this purpose Dosages and method of administration are given in Part 1 Some patients will require antibiotic therapy with penicillin aureomycin chloramphenicol or terramycin given in the manner and dosage recommended in Part 1

effects than morphine Tolerance to metopon is developed slowly and lost rapidly It exerts a long continued analgesic effect and usually should not be given routinely but only as demanded by the patient to control pain Unfortunately some patients are nauseated, constipated, and on the whole do not respond well to this drug

Also in this category are dihydromorphinone (Dilaudid) hydrochloride and methorphinan (Dromoran) hydrochloride Both of these are powerful analgesics that exert a primarily analgesic effect without much sedation Dilaudid is given in a dose of 2 mg subcutaneously at 4 hour intervals while Dromoran is given in a dose of 2 5 to 5 mg subcutaneously at 6- to 8 hour intervals While both have a mild euphoric effect, it is not nearly as pronounced as that of morphine For the most part, the two have the undesirable effects of morphine and unless their non sedation-producing property is highly desirable, they have no real advantage over morphine

Of all the narcotic analgesics, morphine remains the best It relieves pain and sedates It also produces euphoria which can be and often is highly desirable for these patients A dose of 8 to 10 mg of morphine sulfate increased to 20 or even 30 mg every 4 hours is often required Usually doses over 20 mg produce such troublesome side effects as to mitigate the good effects The nausea and vomiting so often produced by morphine can sometimes be avoided if a small (6 to 8 mg) dose is given This is insufficient to stimulate the vomiting center in the central nervous system to action and the depressing effect that follows it after approximately 1 hour makes the center resistant to larger (15 to 20 mg) doses

Morphine should not be used to initiate analgesic therapy, but should be held in reserve for the more serious pain and mental agitation or depression that will appear as the disease progresses However its use should never be withheld when pain is not controlled by other means or where the euphoric effect may save the patient from suffering Addiction is not a major problem in these patients and when present it can be controlled by alternating morphine with methadone A dose of methadone representing one fourth the dose of morphine can usually be substituted for the morphine without causing any withdrawal symptoms or serious interference in the treatment of the patient After 10 days to 2 weeks the addiction to morphine is lost and the patient may be shifted back to morphine if desired

This procedure is also desirable in treating the problem of tolerance

In the treatment of *advanced unoperable or recurrent mammary carcinoma* in the female occuring prior to menopause during menopause and up to 10 years after menopause best results are usually secured by bilateral oophorectomy or radiation castration and the intramuscular administration of 150 to 300 mg of testosterone propionate weekly In patients who have been castrated and who are 10 years postmenopausal excellent results especially in improvement in soft tissue metastases is obtained from the estrogenic hormones Diethylstilbestrol 5 mg 3 times a day by mouth after meals estrone sulfate (Premarin) 10 mg 3 times a day by mouth after meals ethinyl estradiol (Estinyl) 1 0 mg 3 times a day by mouth are all satisfactory oral preparations In some patients there seems to be less nausea and other side effects when the naturally occuring hormones estrone sulfate and ethinyl estradiol are used When an intramuscular preparation is required estradiol (Ovocylin) dipropionate in a dose of 5 mg intramuscularly 3 times a week gives excellent results Whenever possible, however the hormones should be given by mouth since they are effective by this route and save the patient the added discomfort and cost of parenteral administration

Some authorities believe that estrogenic hormones can be given with good effect when the patient is only 5 years postmenopausal or over 60 years of age Undoubtedly there are many cases in this category who are distinctly benefited but more recent evidence shows that there is a greater incidence of acceleration of tumor growth and a lower incidence of objective improvement when estrogens are given on the basis of these criteria rather than on the basis of 10 years postmenopausal

In general sex hormone therapy should not be commenced until the maximum benefit has been secured from castration When regression following castration ceases and evidence of progression appears or if after 2 or 3 months it is apparent that no regression is taking place sex hormone therapy should be initiated The expected objective improvements should include the restoration of normal bony structure calcification of osteolytic metastases no increase in size or number of metastatic lesions in bone decrease in the size of the lesions and no increase in size or number of the lesions in soft tissue Usually when a patient is receiving androgen therapy the hemoglobin hematocrit and red blood cell values all improve while on estrogens these values tend to drop even though objective improvement is occurring

Therapy with these hormones should be continued as long as there is evidence of regression or no sign of progression Recent evidence in

Specific measures These consist of agents such as nitrogen mustard, radioactive iodine, and the steroid hormones Radiation therapy and palliative surgery are also important adjuncts in the treatment of these patients Unfortunately, carcinomas are not sensitive to folic acid antagonists and similar agents, which are so helpful in the treatment of blood dyscrasias

Nitrogen mustard (Mustargen), given in a daily intravenous dose of 0 4 mg per kilogram of body weight on successive days for - to 4 days according to the technique outlined in detail for the treatment of Hodgkins Disease is frequently helpful in relieving distress from a bronchogenic carcinoma Approximately 50 per cent of these tumors will show some palliative response to this therapy

Radioactive iodine is a very useful agent in the treatment of thyroid carcinoma The isotope I^{131} has a half life of 8 days and its distribution in the body follows that of the natural pattern of iodine—which of course leads to heavy concentration in thyroid tissue If radioactive iodine is given to patients with carcinoma of the thyroid before metastases occur and after thorough surgical removal of the tumor, recurrences are unlikely Unfortunately only approximately 15 per cent of metastatic thyroid carcinomas take up sufficient isotope to receive therapeutically effective doses However, surgical removal of the main thyroid mass or radio iodine destruction of the thyroid usually augments considerably the absorption of the isotope into metastatic tissue It is estimated that following these procedures approximately 50 per cent of the metastatic tissue will then take up sufficient radio-iodine to be affected by the radioactivity Dosage should be determined by one skilled in the technique of isotope therapy It varies from single doses of 20 to 150 millicuries Doses above 60 millicuries may cause radiation sickness

Steroid hormones, consisting of androgen, estrogen corticotropin, and cortisone have a very useful place in the treatment of carcinomatosis The sex hormones in particular when properly used afford considerable relief for many patients with mammary and prostatic carcinomas They exert a striking effect on osseous and soft tissue metastatic lesions which contributes materially to the management of the disease Unfortunately they do not prolong life to any extent but they do contribute much to the control of pain the relief of mechanical disorders produced by tumor masses, and the amelioration of osseous lesions with their attendant pain and danger of hypercalcemia or pathological fracture

dence that the hormone is accelerating the process and that it should be stopped. When hypercalcemia appears, a diet containing 200 mg of calcium or less and a fluid intake of 3000 to 4000 cc should be given in order to prevent the development of urinary tract calculi.

The serum alkaline phosphatase level is useful in following therapy. It is usually slightly elevated in the presence of osseous metastases but is moderately to highly elevated with liver metastases. When there is osseous involvement, a rise of more than 50 per cent in serum alkaline phosphatase occurring within a month after initiating hormone therapy usually indicates a good response to the hormone and as therapy continues the level gradually falls over a 6 month period. If it remains low after this interval or if a sudden rise occurs, it can mean a reactivation of tumor growth. Patients with liver metastases who show a fall in serum alkaline phosphatase are responding well to the hormone. Apparently patients with liver metastases who are jaundiced show a more satisfactory response than those without jaundice. In these cases hepatomegaly decreases, jaundice and ascites if present disappear.

On sex hormone therapy most successfully responding cases will show objective improvement within 3 months. Improvement has occurred however as early as 10 days or as late as a year. Therefore a decision to stop therapy should not be made hastily unless obvious acceleration is seen. Usually it takes weeks or months to ascertain the true action of the hormone. Once objective improvement has occurred it may continue for a long time or be lost in a period of a few weeks. On the whole improvement usually continues for 6 months. A range of 1 to 40 months has been reported. Once the tumor regresses on a hormone and then begins to show signs of progression that hormone should be discontinued and the status of the tumor observed. Frequently improvement will be observed after stopping the hormone. When this regression has ceased the patient should then be given a hormone antagonistic to the one previously used. For example, when the patient has been receiving an androgen, an estrogen should be given.

Males with inoperable or metastatic mammary carcinoma should receive a bilateral orchiectomy.

Carcinoma of the Prostate. This carcinoma, like mammary carcinoma, shows a decided response to sex hormone therapy. Approximately 75 per cent of patients with inoperable recurrent or metastatic carcinoma of the prostate are markedly benefited by castration followed by estrogenic therapy. Orchiectomy is favored by many and seems to give

dicates that androgen therapy brings about objective improvement in approximately 24 per cent of patients with soft-tissue lesions and in 20 per cent of patients with osseous lesions, while estrogen therapy will improve 40 per cent of those with soft-tissue lesions and 30 per cent of those with osseous lesions. When progression becomes evident shortly after the initiation of hormone therapy or returns after a period of regression or stasis, the hormone in use should be discontinued, as it has exerted its maximum benefit and further therapy with it at this time is useless and may even be harmful.

These hormones relieve pain in approximately 65 per cent of patients and, when used in conjunction with analgesics as recommended, great relief from suffering is obtained. Other symptoms, such as anorexia, nausea, vomiting, cough, dyspnea, and general fatigue, are also relieved, but usually not as strikingly as is the pain. Patients with osseous metastatic lesions frequently have an initial period of 2 to 3 weeks of increased pain after hormone therapy is started, but this usually subsides and the expected good results ensue.

Patients on hormone therapy must be observed closely, since the use of these agents leads to sodium retention and fluid accumulation that can be of sufficient degree, depending on the physiological status of the patient, to produce cardiac decompensation with pulmonary congestion, peripheral edema, and ascites. This can be corrected by a diet containing 0.5 gm. or less of sodium, mercurial diuretics, and digitalis as recommended for cardiac failure. Administration of estrogens leads to breast enlargement, pigmentation of the areola, and at times to uterine enlargement. When these hormones are discontinued there is a tendency for uterine bleeding which may consist of spotting or may be a moderate flow. When necessary, ergonovine (ergotrate) maleate, 0.2 mg. given by mouth, will usually control this bleeding.

Androgen therapy produces virilization consisting of deepening voice, hirsutism, acne, increased libido, and hypertrophy of the clitoris, but usually these changes are not serious enough to warrant cessation of therapy.

Hypercalcemia from tumor involvement of the bone with subsequent lysis occurs in a small percentage of patients and is corrected when therapy is effective. Serum calcium must be observed carefully, since an increase or the appearance of hypercalcemia for the first time in patients on hormone therapy may indicate that the hormone is no longer effective and that it may be harmful. If hypercalcemia occurs, it is evi-

dence that the hormone is accelerating the process and that it should be stopped When hypercalcemia appears, a diet containing oo mg of calcium or less and a fluid intake of 3000 to 4000 cc should be given in order to prevent the development of urinary tract calculi

The serum alkaline phosphatase level is useful in following therapy It is usually slightly elevated in the presence of osseous metastases but is moderately to highly elevated with liver metastases When there is osseous involvement, a rise of more than 50 per cent in serum alkaline phosphatase occurring within a month after initiating hormone therapy usually indicates a good response to the hormone and as therapy continues the level gradually falls over a 6 month period If it remains low after this interval or if a sudden rise occurs it can mean a reactivation of tumor growth Patients with liver metastases who show a fall in serum alkaline phosphatase are responding well to the hormone Apparently patients with liver metastases who are jaundiced show a more satisfactory response than those without jaundice In these cases hepatomegaly decreases jaundice and ascites if present disappear

On sex hormone therapy most successfully responding cases will show objective improvement within 3 months Improvement has occurred however as early as 10 days or as late as a year Therefore a decision to stop therapy should not be made hastily unless obvious acceleration is seen. Usually it takes weeks or months to ascertain the true action of the hormone Once objective improvement has occurred it may continue for a long time or be lost in a period of a few weeks On the whole improvement usually continues for 6 months A range of 1 to 40 months has been reported Once the tumor regresses on a hormone and then begins to show signs of progression that hormone should be discontinued and the status of the tumor observed Frequently improvement will be observed after stopping the hormone When this regression has ceased the patient should then be given a hormone antagonistic to the one previously used For example when the patient has been receiving an androgen an estrogen should be given

Males with inoperable or metastatic mammary carcinoma should receive a bilateral orchiectomy

Carcinoma of the Prostate This carcinoma like mammary carcinoma, shows a decided response to sex hormone therapy Approximately 75 per cent of patients with inoperable recurrent or metastatic carcinoma of the prostate are markedly benefited by castration followed by estrogenic therapy Orchiectomy is favored by many and seems to give

to 0 5 gm a day in the diet as recommended for heart failure

The hormone should be continued as long as improvement is occurring or the carcinoma is held in check

The fact that the adrenal cortex is a source of extragonadal androgen has lead to total adrenalectomy as a further measure in the removal of androgen hormones Preliminary work indicates that it may have value Further studies are necessary before it can be determined whether or not adrenalectomy will be an important or useful procedure in the treatment of these cases Since the advent of cortisone adrenalectomy is no longer the terribly difficult and dangerous procedure that it was formerly

There is still too little experience with the use of progesterone anhydrohydroxy progesterone and testosterone to draw any definite conclusions in regard to their values They have been used in a few hopeless cases with reported success, but until more data is accumulated they cannot be recommended

Corticotropin or cortisone, although not giving much in the way of objective improvement can be helpful in certain cases of advanced carcinoma They increase the appetite and seem to help certain patients considerably for a temporary period Recent limited experience with cortisone and testosterone given together indicates definite value in the treatment of metastatic breast cancer Cortisone 100 mg orally for 3 or 4 days followed by 50 mg a day suppresses adrenal cortical activity and apparently enhances the value of testosterone

Radiation therapy, consisting of roentgen ray irradiation or interstitial radium therapy has great value in the treatment of carcinoma For tumors such as epidermoid carcinoma of the oral cavity nasopharynx and skin, it is frequently the only acceptable method of treatment Carcinoma of the bladder and uterine cervix also may usually be placed in this category Radiation is useful as a palliative measure in relief from symptoms caused by metastatic lesions It can be used to give relief from the pain of bone metastatic lesions heal skin ulceration shrink greatly enlarged lymph nodes, and reduce tumor masses

This treatment should be given only by those experienced in the technique The therapist, and the intelligence and experience he brings to bear on the problem, are much more important than the machine Each case is an individual problem and dosage length of therapy and portals used must be carefully decided if maximum benefit is to be obtained Patients must be informed about the changes produced by irradiation in the individual These may be of minor proportions or may consist of serious nausea vomiting nutritional deficiency and even

somewhat better results than castration by radiation or suppression by estrogens Orchiectomy is a simple procedure, insures complete cessation of testicular activity and certainly should always be done if the case is advanced or there are metastases It has the disadvantage of the attendant psychological shock, which may be severe in certain patients Usually, however, there is seldom any serious objection to it Unless facilities and skilled personnel are available for proper radiation therapy, there is the possibility that there will be incomplete suppression of activity with radiation and, indeed some feel that complete suppression is never obtained by this procedure Patients with prostatic carcinoma who do not have metastases may be given estrogen therapy initially and then orchiectomy later if there is a failure to respond to the hormone or a recrudescence occurs after an initial response to estrogen

Estrogen therapy is given in the form of diethylstilbesterol, 5 to 15 mg daily by mouth, ethinyl estradiol (Estinyl), 0 5 to 3 0 mg by mouth daily, and chlorotrianisene (Tace), 24 mg by mouth daily The last apparently has some advantage over the other estrogens in that preliminary observations indicate that it does not stimulate the adrenal cortex or pituitary to as great a degree and consequently androgens are not produced by these organs in as great amount

Patients with prostatic carcinoma responding satisfactorily to orchiectomy or estrogen therapy experience a remarkable relief of pain, gain in weight and the primary and metastatic lesions shrink Those with urinary retention due to the carcinoma when placed on catheter drainage and estrogen therapy usually show excellent improvement and in many cases surgical intervention can be avoided

Prostatic carcinoma that may at first appear to be inoperable may respond so remarkably to estrogen therapy as to become amenable to surgery There are already a number of reports of successful surgery after hormone therapy had converted the tumor into one where a successful radical perineal prostatectomy could be done

The acid phosphatase usually abnormally high in well advanced and metastic carcinoma of the prostate generally shows a decided decrease following orchiectomy or estrogen therapy Conversely, a sharp increase in acid phosphatase implies the spread of the lesion and a continued upward trend suggests further metastatic involvement

Estrogens usually produce breast enlargement and can cause anorexia, nausea and vomiting as well as sodium and fluid retention The hormone should be given in divided doses usually twice a day after breakfast and at bedtime Fluid retenion should be treated with sodium restriction

Inoperable Carcinoma

1 Council on Pharmacy and Chemistry Estrogens and Androgens in Mammary Cancer Progress Report *Jour Amer Med Assoc*, 1949, 140 p 1214
2 ESCHER G C Hormone Therapy in Advanced Mammary Cancer *Med Clin No Amer* May 1952 p 681
3 LEMON H M Treatment of Inoperable Carcinoma *Med Clin No Amer* September 1951 p 1361
4 NATHANSON I T and KELLEY R M Hormonal Treatment of Cancer *N E J Med*, 246 1952 pp 135 180
5 SALTER W T *Textbook of Pharmacology* W B Saunders Co 195
6 WILHELM S F Carcinoma of the Prostate *Med Clin No Amer*, May 1952 p 689

mental depression As yet there is no specific treatment for the control of irradiation sickness but the measures recommended on page 645 are helpful and will do much to lessen the effect of irradiation

Surgery is most helpful in properly selected patients The rapid advances in technique now permit far more extensive resections than were formerly possible and no patient should be considered inoperable until a surgeon skilled in the surgery of the involved organ or tissue considers the carcinoma too advanced for direct attack and removal Even advanced cases can be ameliorated by skilled surgery Obstructed bowels, urinary tracts bile ducts and pancreatic ducts can frequently be reconstructed so as to give the patient much comfort and a longer life Removal of a diseased lung has given patients many months of remission and comfort when an advanced bronchogenic carcinoma was threatening their existence through infection and hemorrhage

Surgical palliative measures such as the destruction of peripheral sensory nerves, posterior rhizotomy or even intermedullary sphinothalamic tractotomy, afford certain patients great relief from pain and should be done before tolerance to morphine has seriously impaired the value of the drug Surgical removal of adrenal glands as a further measure in hormone alteration is proving of value in metastatic carcinoma of the prostate and shows promise in a few patients with carcinoma of the breast on whom it has been tried

BIBLIOGRAPHY

Diseases of Undetermined Etiology

1 BRUNSTING L A Acute Disseminated Lupus Erythematosus," *Med Clin No Amer* 1951 xxxv p 339

2 FORSHAM P ACTH and Cortisone in Therapy, *Med Clin No Amer* Sept. 1951, p 1229

3 HUEBNER R J BEEMAN, E A COLE R, M BEIGELMAN P M and BELL J A Medical Progress The Importance of Coxsackie Viruses in Human Disease Particularly Herpangina and Epidemic Pleurodynia *N E J Med* 247 1952 p 249 285

4 OGRYZLO M and GRAHAM W Reiter's Syndrome Effect of Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone *Jour Amer Med Assoc* 1950 cxliv p 1 39

5 STRANGWAY W and STRANGWAY A Ascorbic Acid Deficiency in the African Disease Onyalai' *Arch Int Med*, 1949, lxxxiii p 372

PART IX

DISEASES DUE TO BITES OF ARTHROPODS AND REPTILES

CHAPTER XXVII

NOXIOUS ARTHROPODS AND VENOMOUS REPTILES

Noxious Arthropods

Only three orders of arthropods are important medically for man *Acarina* (mites and ticks) *Araneida* (spiders) and *Scorpionida* (scorpions)

Mites

Several different varieties of mites attack man and all produce itching and dermatitis Treatment depends on the type of mite and on the lesions produced

Chiggers, Copra Itch, Grocer's Itch, Straw Itch Simple dermatitis produced by mites such as straw itch grocer's itch copra itch and chigger bites is best prevented by dusting the exposed skin of anyone handling grains and foods or in infested fields with a powder containing 5 per cent Chlorophenothane [DDT] Impregnation of clothing with a 5 per cent solution of dimethylphthalate dibutylphthalate or benzyl benzoate will also kill mites before they have an opportunity to bite

Once mites are on the skin they should be destroyed by dusting with a powder containing 5 per cent Chlorophenothane or by the application

given If the source of the infection is not known the patient should be informed about the way the disease is spread and advised about avoiding contact with individuals and articles likely to be contaminated When there is repeated reinfection and the source cannot be determined it may be necessary to use a 0 5 per cent Chlorophenothane [DDT] ointment spread thinly over the patient s hands or a powder containing 5 per cent Chlorophenothane until the source can be eliminated Care must be taken to avoid toxic effects from this drug The use of a soap containing 5 per cent tetraethylthiuram monosulfide (Tetmosal) is also of assistance in preventing infection

Prophylaxis Prevention should consist of avoiding contact with the mites in straw on food in the fields and on infected individuals A 5 per cent Chlorophenothane powder a 0 5 per cent ointment of it or a mixture of benzyl benzoate soft soap and isopropyl alcohol in equal parts will when applied to the skin destroy mites already on the body Impregnation of clothing with either 5 per cent dimethylphthalate 5 per cent dibutylphthalate or benzyl benzoate will destroy mites before they can get on the body and will serve as excellent protection

Ticks

Not only are ticks a serious menace as carriers of disease but there are certain varieties whose bite produces severe local lesions as well as serious illness

Bites by ticks of the Ixodidae family genus Dermacentor (D andersoni, D variabilis) and genus *Amblyomma Americanum* (Lone Star tick) can be serious because of the development of local infection lymphangitis severe pain fever and paralysis

Treatment should consist of prompt and careful removal of the tick with special caution being taken not to leave the mouth parts embedded in the skin since infection and irritation will result if they are not removed Of the several methods for the removal of ticks the simplest is the application of heat near the tick so that it is forced to detach its mouth parts and seek a cooler area Heat may be applied in many ways — from a lighted cigarette an electric light bulb a magnifying glass or the hot head of a quickly extinguished match Gasoline turpentine ether and alcohol also will serve to force release of the mouth parts The tick should then be picked up with forceps and destroyed The wound

of an ointment containing 0 5 per cent of the drug Not more than 15 gm should be used at any one time It should be applied thoroughly to hairy areas Sulfur ointment U S P, or a mixture of equal parts of soft soap benzyl benzoate and isopropyl alcohol can also be used with good effect If there is local itching, 2 per cent tripelennamine (Pyribenzamine) hydrochloride cream applied to the area will give considerable relief Infection should be treated with the appropriate antibiotic or with sulfadiazine Infected clothing should be thoroughly cleaned to kill all mites before it is worn again

Scabies The itch mite *Sarcoptes scabiei*, is the most important of the mites that attack man since it is common, rapidly disseminated and causes the severe dermatitis, scabies At times the spread of scabies reaches epidemic proportions and creates widespread distress The patient with severe scabies should receive when indicated, phenobarbital 0 1 gm for sedation diphenhydramine (Benadryl) hydrochloride, 50 mg every 4 hours for itching and penicillin or sulfadiazine, or one of the broader spectrum antibiotics if necessary to control infection The local attack on the parasite is then begun A warm soaking bath to soften the epidermis and vigorous scrubbing with soft soap and a brush to open the vesicles should be followed by the application of a lotion consisting of equal parts of soft soap benzyl benzoate and isopropyl alcohol This lotion should be applied thoroughly to all areas except the face and should be rubbed in with a stiff brush Two complete applications should be made The patient then puts on the same clothing he wore previously and sleeps in the same bed linen The old clothing and bed linen are removed 24 hours later and sterilized and the patient puts on fresh clothing If the first treatment fails to remove all of the parasites a second course of treatment should be given promptly, followed by a third if necessary Repeated applications should be avoided when possible, however because they may lead to skin irritation

Sulfur can be used in the treatment of scabies but it is slow, it may produce dermatitis and is so disagreeable that it has been largely replaced by benzyl benzoate

Since it is useless to treat the individual patient unless the source of the infection is controlled a determined effort should be made to locate the source and eliminate it. The patient s family is likely to be infected also, and consequently must be investigated and subjected to the same treatment the patient is receiving Careful instructions concerning the sterilizing of clothing, bed linen, towels and similar articles must be

should be applied the site incised and the poison removed by suction If available, specific antivenin should be given intramuscularly in a dose of 2 5 cc repeated in 1 to 2 hours if necessary The usual procedures to determine sensitivity to horse serum should be carried out Epinephrine hydrochloride 1 1000 and antihistaminics should be given immediately in case of reactions and should be administered as described for serum sensitivity under Diphtheria

Muscle spasm with consequent severe pain is relieved by calcium gluconate 10 cc of a 10 per cent solution given intravenously and repeated in 1 hour if indicated This relaxes spasms and relieves cramps Amyl nitrate inhalation 0 2 to 0 3 cc may give temporary relief

Meperidine (Demerol) hydrochloride 100 to 150 mg intramuscularly or methadone 10 mg intramuscularly will give considerable relief from pain and muscle spasm Morphine sulfate 8 mg hypodermically, may also be given but it does not relax smooth muscle spasm

Mephenesin (Tolserol) 1 0 gm given orally and repeated every 4 hours if necessary may prove helpful in relaxing muscle spasm

Neostigmine (Prostigmine) methylsulfate 1 2000 in a dose of cc given intravenously with atropine sulfate 0 4 mg is helpful in relaxing muscle spasm as is magnesium sulfate as a 10 per cent solution 20 cc given intravenously

Hot baths or hot packs and sedatives such as secobarbital (Seconal) 0 1 gm or pentobarbital (Nembutal) 0 1 gm also are useful supportive measures when given with an effective analgesic

Prophylaxis Care should be taken in using old outdoor privies handling old lumber picking grapes or tomatoes and in general handling material likely to harbor the spider Creosote sprayed under toilet seats and into areas where the spiders are likely to locate is effective Spraying or dusting basements outhouses privies and such likely spider habitats with 10 per cent Chlorophenothane [DDT] or a 5 per cent spray in kerosene is very effective

The bite of the tarantula while painful is not very toxic Treatment should begin with immediate reassurance of the patient regarding the minor nature of such a bite If pain is severe and the patient is apprehensive morphine sulfate 8 mg hypodermically will give excellent results The bite should be cleaned carefully and a local antiseptic applied

Prophylaxis Care should be exercised when handling fruit shipped from tropical areas

site should be washed with soft soap and water, touched with a tooth pick dipped in phenol or with a silver nitrate stick, and then covered with an ointment containing either aureomycin, bacitracin, or sulfadiazine or painted with a mild tincture of iodine Severe itching will be promptly relieved by the application of a cream containing tripelennamine (Pyribenzamine) hydrochloride, 2 per cent If lymphangitis or evidence of serious infection appears, penicillin, sulfadiazine, or other antibiotics depending on the organism should be given in full dosage Fever, pain and paralysis when present, usually disappear with the removal of the ticks

Prophylaxis In tick-infested areas boots and adequate clothing should be worn so that there is no opportunity for the ticks to get onto the body Dusting 10 per cent Chlorophenothane [DDT] powder once a day on both the inside and the outside of clothing is effective Careful watch for ticks should be maintained, and the body should be searched at least twice a day special attention being given to the perineal region the axillae, the areas behind the ears and between the toes, and the scalp Dogs should be deticked carefully before being permitted to play with children or to come into the house Chlorophenothane is effective against dog ticks a half teaspoonful of the 10 per cent powder dusted into the fur in the neck and on the back is effective Cats should be treated likewise using a correspondingly smaller amount of the 10 per cent powder It should also be dusted in areas frequented by such pets Heavily contaminated areas can be dusted with Chlorophenothane with excellent results in reducing the tick population

Spiders

There are only two spider groups that are of consequence as far as man is concerned These are the black widows (*Latrodectus*), especially *Latrodectus mactans*, and the several species of tarantulas the most venomous being the black tarantula of Panama *Sericopelma communis*

Arachnidism of severe degree is produced by the bite of the black widow Treatment is not entirely satisfactory but when it is carried out promptly, it will do much to alleviate the severe muscle spasm and pain Cortisone in a dose of 200 to 300 mg or corticotropin 75 to 100 mg intramuscularly should be given If the bite is on an extremity or in such a location that it can be isolated from circulation, a tourniquet

Ants, Bees, Hornets, and Wasps

When these insects of the order *Hymenoptera*, sting man they deposit formic acid and a toxic protein alkaline in nature which when acted upon by the formic acid produces a most painful edematous lesion Treatment should consist of the prompt removal of the sting if it has been left at the site as is commonly the case This is best done by gentle pressure and by manipulating the tissue rather than by attempting to pull out the barbed shaft by direct traction since pressure on it will usually force more poison into the tissue or break off the shaft Prompt application of hot packs a paste of sodium bicarbonate repeated several times or a strong ammonia solution will give considerable relief Repeated applications of a per cent tripelennamine (Pyribenzamine) hydrochloride cream well massaged into the area, are effective in decreasing pain swelling and itching Tripelennamine (Pyribenzamine) hydrochloride or diphenhydramine (Benadryl) hydrochloride, 50 to 100 mg given orally and repeated every 3 hours is helpful in controlling allergic phenomena If severe allergic manifestations appear epinephrine hydrochloride 1 1000 should be given subcutaneously in a dose of 0 5 cc

Acetylsalicylic acid 0 3 to 0 6 gm may be given for pain and repeated in 3 to 4 hours if necessary Severe pain produced by many stings may require methadone, 5 to 10 mg given intramuscularly for relief

Prophylaxis Destruction of wasp nests or spraying them with a mixture of 10 per cent Chlorophenothane (DDT) in kerosene is effective If individuals are known to be sensitive to bee stings they may be desensitized by the use of a whole bee extract given in the manner described for hay fever desensitization This procedure gives considerable cross protection against other members of the *Hymenoptera* order Care in handling bees will avoid many stings Do not brush slap blow on or in any way excite or injure the insect Some protection is afforded by wearing light colored clothing when one is around bees The liberal use of Chlorophenothane will destroy insects of this order whenever they constitute a nuisance

Bedbugs (Cimex Lectularius)

The bite of this insect is very irritating to some individuals and local infection with ulceration may result Treatment should consist of the

Scorpions

Stings by the poisonous scorpions, especially *Centruroides suffusus, Tetynus serrulatus,* and *Buthus quinquestriatus,* while not usually fatal to adults are very serious in children and result in a high death rate Treatment should consist of applying a tourniquet, incising the sting site and applying suction to remove venom Cortisone or corticotropin as recommended for spider bites should be given Species specific anti venin if available will prove helpful, also, the application of an ice cube or spraying with ethyl chloride will give some relief from local pain

Sedation with phenobarbital 0 1 to 0 2 gm, or pentobarbital, 0 1 to 0 2 gm is indicated For convulsions sodium phenobarbital is to be given subcutaneously as a 20 per cent solution in distilled water, in dosage of 0 1 to 0 3 gm Intravenous glucose, 10 per cent in saline, should be started immediately and plasma may be used if shock is present Hypotension in adults should be treated either with 1 per cent phenyl ephrine (Neosynephrine) hydrochloride solution, 0 5 to 1 0 cc intramuscularly repeated in 15 minutes to half an hour as indicated, or with hydroxyamphetamine (Paredrine) hydrobromide, 10 to 20 mg by mouth Epinephrine hydrochloride, 1 1000, although less effective, also may be given intramuscularly to adults in a dose of 0 5 cc Smaller doses of these drugs are indicated for children

If apprehension and pain are severe a hypodermic of morphine sulfate 8 mg, will give relief pentobarbital (Nembutal), 0 1 to 0 2 gm, with methadone 5 to 10 mg will also control the pain

Prophylaxis Care in handling lumber debris and other material likely to harbor the scorpion should be observed Protection of the feet and ankles in endemic areas is important Shoes and clothing should be thoroughly shaken out before they are worn Where scorpions are pests their numbers can be reduced by the presence of chickens which relish them as a food Ivy or similar thick clinging vines serve as hiding places for scorpions

Common Insects

This class of arthropods is not only the largest but also the most important medically Of the many species ants, bedbugs bees, caterpillars, fleas flies hornets leeches lice mosquitoes and wasps are most interesting medically

itching is a factor 2 per cent tripelennamine (Pyribenzamine) hydrochloride cream will give relief Secondary infections should be treated as described for local infections

The chigoe flea (sand flea chigger jigger) penetrates the skin usually of the feet, where it appears like a small pustule It should be removed carefully under aseptic conditions by using a sterile needle to enlarge the entrance hole of the flea and then applying gentle pressure to force the flea out *in toto* Tincture of benzylkonium (Zephiran) chloride 1 1000 or 3 per cent tincture of iodine should be applied to the wound

Prophylaxis Dusting with 5 to 10 per cent Chlorophenothane (DDT) will destroy fleas on man and animals In addition dusting rugs, furniture and other possible habitats with it will quickly eliminate the fleas Application of essential oils or repellants, such as 2 ethylhexanediol-1,3, to the feet will prevent sand fleas from attacking the bare feet in endemic areas

Flies

The order *Diptera* has many medically important species that attack man The lesions produced arise essentially from bites and myiasis the invasion of body cavities or skin by larvae

Treatment of bites should consist of applying sodium bicarbonate paste or ammonia water to relieve the pain and touching the area with 1 1000 tincture of benzylkonium (Zephiran) chloride or 3 per cent tincture of iodine Itching is alleviated by applying 2 per cent tripelennamine (Pyribenzamine) hydrochloride cream If the site becomes infected it should be treated as described for local infections

Cutaneous Myiasis Cutaneous myiasis produced by larvae of the human botfly *Dermatobia hominis*, may be treated by anesthetizing the area with 2 per cent procaine hydrochloride take care to instill the anesthetic into the central areas of the furuncle so as to anesthetize the parasites and then incise the furuncle and remove the parasites The area should be treated as described for local infections

Larvae migrans type of cutaneous myiasis produced by *Gasterophilus intestinalis* should be treated by surgical extraction of the parasite after local anesthesia Antihistiminic ointments will relieve much of the itching Tumbu fly *(Cordylobia anthropophaga)* larvae invasion of the skin is treated by immersing the lesion in water thus removing the oxygen supply The spiracles then emerge and the larvae can be pressed out

Scorpions

Stings by the poisonous scorpions, especially *Centruroides suffusus, Tetyrus serrulatus*, and *Buthus quinquestriatus*, while not usually fatal to adults are very serious in children and result in a high death rate Treatment should consist of applying a tourniquet, incising the sting site and applying suction to remove venom Cortisone or corticotropin as recommended for spider bites should be given Species specific anti venin if available, will prove helpful also, the application of an ice cube or spraying with ethyl chloride will give some relief from local pain

Sedation with phenobarbital 0 1 to 0 2 gm, or pentobarbital, 0 1 to 0 2 gm is indicated For convulsions sodium phenobarbital is to be given subcutaneously as a 20 per cent solution in distilled water, in dosage of 0 1 to 0 3 gm Intravenous glucose 10 per cent in saline should be started immediately and plasma may be used if shock is present Hypotension in adults should be treated either with 1 per cent phenyl ephrine (Neosynephrine) hydrochloride solution, 0 5 to 1 0 cc intramus cularly repeated in 15 minutes to half an hour as indicated, or with hydroxyamphetamine (Paredrine) hydrobromide, 10 to 20 mg by mouth Epinephrine hydrochloride 1 1000 although less effective, also may be given intramuscularly to adults in a dose of 0 5 cc Smaller doses of these drugs are indicated for children

If apprehension and pain are severe a hypodermic of morphine sul fate 8 mg, will give relief pentobarbital (Nembutal), 0 1 to 0 2 gm with methadone 5 to 10 mg will also control the pain

Prophylaxis Care in handling lumber debris and other material likely to harbor the scorpion should be observed Protection of the feet and ankles in endemic areas is important Shoes and clothing should be thoroughly shaken out before they are worn Where scorpions are pests their numbers can be reduced by the presence of chickens which relish them as a food Ivy or similar thick clinging vines serve as hiding places for scorpions

Common Insects

This class of arthropods is not only the largest but also the most im portant medically Of the many species ants bedbugs bees caterpillars fleas, flies hornets leeches lice, mosquitoes and wasps are most interest ing medically

soap and water and while still damp, is combed with a fine toothed comb to remove dead lice and nits Clothing must be disinfected by heat or dusted with Chlorophenothane powder

Two per cent tripelennamine (Pyribenzamine) hydrochloride cream or diphenhydramine (Benadryl) hydrochloride cream will give relief from itching A warm bath to which sodium bicarbonate has been added to make the water all aline is also soothing Itching may be relieved by applying a mixture of 5 per cent ethylaminobenzoate U S P (Benzocaine), 2 per cent methyl salicylate and 0 5 per cent salicylic acid in 70 per cent alcohol

Prophylaxis Ordinary cleanliness usually suffices In crowded con ditions, where clothing must be worn for long periods of time, in cold climates, and in contact with carriers, infestation is likely to occur and must be prevented by dusting the clothing and body with 10 per cent Chlorophenothane powder in pyrophylite every 2 weeks Removal of clothing at least once in 24 hours will prove helpful Baths and steam sterilization of clothing are also effective

Mosquitoes

Mosquitoe bites are usually of minor significance but they can, in certain individuals, cause considerable local swelling and itching There is apparently a mild allergy developed in these persons

Rapid relief from the swelling and itching will be obtained by the application of a 2 per cent antihistaminic cream Local infections resulting from scratching should be treated as previously described

Prophylaxis There are several very effective mosquito repellants that remain active for from 4 to 6 hours after application Three of these agents are indalone dimethylphthalate and 2 ethylhexanediol 1-3

Leeches

Externally attached leeches should be removed by anesthetizing them with a touch of 10 per cent cocaine solution or by applying 95 per cent alcohol vinegar or a strong salt solution Touching them with a lighted cigarette or a cautery tip will also dislodge them The site should be cleaned and to control bleeding touched with a styptic pencil or pow dered alum Tincture of benzylkonium (Zephiran) chloride 1 1000

application of 3 per cent aureomycin or bacitracin ointment, or of touching the site with 3 per cent tincture of iodine and applying 2 per cent tripelennamine (Pyribenzamine) hydrochloride cream Antihistaminic ointment will reduce markedly the local itching and irritation and will thus help prevent the infection that usually results from scratching

Prophylaxis Dusting beds mattresses, springs, and rooms with Chlorophenothane [DDT] powder, 5 to 10 per cent, will effectively eliminate this pest

Caterpillars

Severe skin irritation and urticaria are produced by several groups of caterpillars by means of poison secreting cells or glands associated with bristles or hollow spines The most serious offenders are the puss caterpillar *(Megalopyge opercularis)* and the brown tail moth *(Megalopyge phalorrhoea)* Treatment should consist of prompt application of a sodium bicarbonate paste or ammonia water, 2 per cent tripelennamine (Pyribenzamine) hydrochloride cream repeated as indicated for itching is helpful in controlling much of the urticaria and severe itching Antazoline (Antistine) hydrochloride 0 5 per cent ophthalmic solution is helpful where the conjunctivae are involved Secondary infections should be treated as previously described

Prophylaxis Destroy the caterpillars by spraying trees and shrubs with lead arsenate and Chlorophenothane [DDT] solution Clothing bedding, and other articles contaminated with caterpillar hairs should be washed or cleaned

Fleas

Only four of the many species of fleas are encountered on man often enough to present a medical problem resulting from their own activity These are *Ctenocephalidea canis*, *Ctenocephelides felis*, *Pulex irritans*, and the chigoe flea, *Tunga penetrana* The last mentioned must not be confused with the mite *Trombicula irritans*, which in the United States is also called red bug' or chigger Other fleas may bite man but they are not common Flea bites may be of little or no significance but they may prove most irritating Treatment should consist of cleansing the bite area and applying a local antiseptic such as 3 per cent tincture of iodine or a 1 1000 tincture of benzylkonium (Zephiran) chloride If

is reason to suppose that a large amount of poison especially neurotoxin has been injected or if the bite has been made by an exceedingly poisonous variety of snake it is wise to apply a second tourniquet proximal to the first and at a point where the arterial blood supply will be impeded In exceptional cases when an exceedingly poisonous snake has bitten a finger, *amputation is justified providing the poison has been localized* by a tourniquet Both the venous and arterial tourniquets must be released for brief periods every 15 to 20 minutes The bite area should then be painted with 3 per cent tincture of iodine, under aseptic conditions crucial incisions one fourth to one half inch deep depending on the depth of the bite are then made through the fang marks The cuts should be irrigated when possible with warm sodium citrate solution to prevent blood clotting this is repeated during the suction period Immediate suction should be made with a suitable apparatus The rubber bulb and metal suction applicator as supplied in snake bite kits a breast pump a suction bulb or suction applied by an irrigating syringe with the tip in the fang openings is excellent In emergencies mouth suction may be used but it carries the hazard of sepsis and there is also the possibility of some of the poison being absorbed through a break in the mucous membranes of the individual applying the suction If mouth suction is used the bite area must be thoroughly irrigated with an antiseptic such as benzylkonium (Zephiran) chloride 1 1000 following the suction Half of a condom used in the mouth for suction prevents absorption of the poison and keeps saliva out of the wound Intermittent suction for from a half to three quarters of an hour should be continued for 12 to 16 hours No local treatment other than repeated irrigations with sodium citrate or local injections of specific antivenin should be given Permanganate crystals or solutions are contraindicated As swelling appears and begins to spread the tourniquet should be moved ahead of it and a series of incisions one fourth inch deep by one fourth inch long should be made around the edge of the advancing edema and suction should be applied

Cortisone 200 to 300 mg or corticotropin 75 to 100 mg intramuscularly should be given promptly If available specific antivenin should also be given immediately The polyvalent North American anti snake bite serum is specific for bites of the rattlesnake copperhead and moccasin The lyovac process insures a stable antivenin at room temperature Specific antivenins are also available for snakes of other regions of the world For bites by small snakes 15 cc of the antivenin given intra

The common cutaneous myiasis produced by various species is to be treated by removing the larvae under aseptic conditions and controlling the local infection

Nasal and oral myiasis should be treated by spraying the larvae with 1 per cent cocaine and the conjunctivae with 1 per cent butacaine sulfate In the nose or ear, ether on a cotton pledget or a 1 per cent solution of chloroform in milk may be applied to the involved area In the nose, shrinking of the mucous membrane with 0 25 per cent phenylephrine (Neosynephrine) hydrochloride is helpful The larvae then may be removed by blowing the nose or by forceps The usual treatment for local infection is indicated

Gastric and intestinal myiasis should be treated by emetics to remove the larvae from the stomach and cathartics to remove them from the intestinal tract

Genito-urinary myiasis is difficult to treat Cystoscopic removal may prove helpful Urinary tract antibacterial therapy is usually sufficient treatment

Prophylaxis Screening sufficient body clothing, protection of wounds and infections by bandages the use of insecticides such as Chlorophenothane [DDT] and insect repellants such as indalone, and the many common measures for fly control are all indicated

Lice

Treatment for the various forms of lice that infest man has been simplified by the discovery of Chlorophenothane [DDT], as this chemical is easily applied and rapidly destroys lice A powder containing 10 per cent Chlorophenotane in pyrophylite will quickly kill all lice whether they are in the hair of the head, on the body or in the pubic hair Dusting should be repeated in a week or ten days to catch any nites that may have hatched Combing with a fine toothed comb, following a shampoo with soap and warm water will hasten the removal of nits and relieve itching Lice in clothing are destroyed by dusting with the powder

Cuprex is also effective especially against head and pubic lice This should be rubbed into the hair care being taken not to get any into the eyes, on the mucous membranes of the urethra labia and anus or on the skin of the face After 2 to 4 hours the hair is washed thoroughly with

is reason to suppose that a large amount of poison, especially neurotoxin has been injected or if the bite has been made by an exceedingly poisonous variety of snake it is wise to apply a second tourniquet proximal to the first and at a point where the arterial blood supply will be impeded In exceptional cases when an exceedingly poisonous snake has bitten a finger amputation is justified providing the poison has been localized by a tourniquet Both the venous and arterial tourniquets must be released for brief periods every 15 to 20 minutes The bite area should then be painted with 3 per cent tincture of iodine under aseptic conditions crucial incisions one fourth to one half inch deep depending on the depth of the bite, are then made through the fang marks The cuts should be irrigated when possible with warm sodium citrate solution to prevent blood clotting this is repeated during the suction period Immediate suction should be made with a suitable apparatus The rubber bulb and metal suction applicator as supplied in snake bite kits *a breast pump a suction bulb or suction applied by an irrigating syringe* with the tip in the fang openings is excellent In emergencies mouth suction may be used but it carries the hazard of sepsis and there is also the possibility of some of the poison being absorbed through a break in the mucous membranes of the individual applying the suction If mouth *suction is used the bite area must be thoroughly irrigated with an anti* septic such as benzylkonium (Zephiran) chloride 1 1000 following the suction Half of a condom used in the mouth for suction prevents absorption of the poison and keeps saliva out of the wound Intermittent suction for from a half to three quarters of an hour should be continued for 12 to 16 hours No local treatment other than repeated irrigations with sodium citrate or local injections of specific antivenin should be given Permanganate crystals or solutions are contraindicated As swelling appears and begins to spread the tourniquet should be moved ahead of it and a series of incisions one fourth inch deep by one fourth inch long should be made around the edge of the advancing edema and suction should be applied

Cortisone 200 to 300 mg or corticotropin 75 to 100 mg intramuscularly should be given promptly If available specific antivenin should also be given immediately The polyvalent North American anti snake bite serum is specific for bites of the rattlesnake copperhead and moccasin The lyovac process insures a stable antivenin at room temperature Specific antivenins are also available for snakes of other regions of the world For bites by small snakes 15 cc of the antivenin given intra

is reason to suppose that a large amount of poison especially neurotoxin has been injected or if the bite has been made by an exceedingly poisonous variety of snake it is wise to apply a second tourniquet, proximal to the first and at a point where the arterial blood supply will be impeded In exceptional cases when an exceedingly poisonous snake has bitten a finger amputation is justified providing the poison has been localized by a tourniquet *Both the venous and arterial tourniquets must be released for brief periods every 15 to 20 minutes* The bite area should then be painted with 5 per cent tincture of iodine under aseptic conditions crucial incisions one fourth to one half inch deep depending on the depth of the bite are then made through the fang marks The cuts should be irrigated when possible with warm sodium citrate solution to prevent blood clotting this is repeated during the suction period Immediate suction should be made with a suitable apparatus The rubber bulb and metal suction applicator as supplied in snake-bite kits a breast pump a suction bulb or suction applied by an irrigating syringe with the tip in the fang openings is excellent In emergencies mouth suction may be used but it carries the hazard of sepsis and there is also the possibility of some of the poison being absorbed through a break in the mucous membranes of the individual applying the suction If mouth suction is used the bite area must be thoroughly irrigated with an antiseptic such as benzalkonium (Zephiran) chloride 1 1000 following the suction Half of a condom used in the mouth for suction prevents absorption of the poison and keeps saliva out of the wound Intermittent suction for from a half to three quarters of an hour should be continued for 12 to 16 hours. No local treatment other than repeated irrigations with sodium citrate or local injections of specific antivenin should be given Permanganate crystals or solutions are contraindicated As swelling appears and begins to spread the tourniquet should be moved ahead of it and a series of incisions one fourth inch deep by one fourth inch long should be made around the edge of the advancing edema and suction should be applied

Cortisone 200 to 300 mg or corticotropin 75 to 100 mg intramuscularly should be given promptly If available specific antivenin should also be given immediately The polyvalent North American anti snake bite serum is specific for bites of the rattlesnake copperhead and moccasin The lyovac process insures a stable antivenin at room temperature Specific antivenins are also available for snakes of other regions of the world For bites by small snakes, 15 cc of the antivenin given intra

in the same manner as described for snakebite Since the poison is at the base of the lower teeth and must flow from there into the wound, the danger is lessened if the lizard is held in an erect position until it can be removed This usually involves rotating both the area and the biting lizard, as the lizard usually bites while on its back

If convulsions appear sodium pentobarbital (Nembutal) 0 2 to 0 3 gm intravenously in a 5 per cent solution, is indicated Corticotropin or cortisone in the dosage recommended for snakebite should be tried The measures advised for snakebite should also be carried out

BIBLIOGRAPHY

1 CLUXTON H E The Treatment of Black Widow Spider Bite and Copperhead Snake Bite with ACTH *Clinical ACTH* ii Mote J P Blakiston 1951 p 455

2 TAYLOR I R Arachnidism ' *Oxford System Med* 1948 v p 966 (27)

venously is sufficient Bites of larger snakes or cases in which there has been delay in treatment may require 30 to 75 cc of antivenin intravenously in adults Children should be given proportionately larger doses since there is more poison to total body weight The patient must be tested first for horse-serum sensitivity This may be done by diluting the serum 1 10 and giving 0 1 cc subcutaneously or by placing a drop in the conjunctival sac If no reactions occur, it is safe to proceed with the serum intravenously If there is a reaction, desensitization must be performed before the serum can be administered If the conjunctival sac test causes much reaction in the eye a drop of 0 5 per cent antazoline (Antistine) hydrochloride ophthalmic solution, will give quick relief

Morphine sulfate 8 mg hypodermically may be given to relieve pain and for sedation Alcohol must be avoided Shock and circulatory collapse should be treated by transfusions of plasma or whole blood If hemorrhages appear, transfusions of whole blood 10 per cent calcium gluconate, 10 cc intravenously vitamin C 1 0 gm orally, and vitamin K, 10 mg intravenously in 10 per cent dextrose infusion, are indicated Respiratory embarrassment, when present should be treated by oxygen inhalation pentamethylenetetrazol (Metrazol), 0 1 to 0 3 gm orally or intravenously, or caffeine sodium benzoate, 0 5 gm subcutaneously or intravenously

If sepsis develops treatment with penicillin streptomycin, or aureomycin should be carried out as described under Bacterial Infections For the prevention of tetanus the usual prophylactic dose of 1500 to 2000 units of anti-tetanic serum should be given Penicillin procaine 300 000 units in aqueous suspension intramuscularly daily for 3 days is also advised

Prophylaxis The wearing of leather high top shoes or leather leggings affords excellent protection Loose heavy trouser legs are of some help and the tropical helmet with its wide brim gives some protection against arboreal snakes In heavily infested areas care should be taken in traveling at night since most snakes are nocturnal in their habits Alertness, careful watch for snakes and the ability to recognize the warning rattle will prevent many bites

Poisonous Lizards

The gila monster of the southwest United States and the beaded lizard of southwest Mexico are poisonous and their bites must be treated

PART X

DISEASES DUE TO PHYSICAL AGENTS AND INTOXICATIONS

CHAPTER XXVIII

EFFECTS OF PHYSICAL AGENTS

Sunstroke Heat Stroke

In sunstroke with its high fever the essential treatment is to lower the body temperature rapidly but by proper measures Too often drastic practices such as ice water enemata may harm the patient rather than relieve him and therefore they are not recommended

The best way to lower the body temperature is to use procedures that uniformly cool the skin surface First the patient should be removed from the hot environment and placed in a cool room If that is not possible shade should be provided Clothing should be removed so that good ventilation is established Repeated cool water sponging of the skin is a good first aid measure

Where ice is available it may be rubbed over the body For the patient with very high body temperature 108 to 112°F careful immersion in ice water from 10 to 30 or 40 minutes has often been done Better results come from sprinkling cold water on a sheet covering the naked patient and blowing air over the wet sheet with an electric fan When the patient's temperature falls to 102 F this procedure should be stopped but it should be repeated if the fever begins to rise Recurrence of fever of 102 to 103 F over the next 2 or 3 days is not uncommon and ordinarily does not require resumption of the ice baths If the temperature falls to subnormal levels acute circulatory collapse may occur this may be avoided by giving the patient a warm tub bath

venously is sufficient Bites of larger snakes or cases in which there has been delay in treatment may require 30 to 75 cc of antivenin intravenously in adults Children should be given proportionately larger doses since there is more poison to total body weight The patient must be tested first for horse-serum sensitivity This may be done by diluting the serum 1 10 and giving 0 1 cc subcutaneously or by placing a drop in the conjunctival sac If no reactions occur, it is safe to proceed with the serum intravenously If there is a reaction desensitization must be performed before the serum can be administered If the conjunctival sac test causes much reaction in the eye, a drop of 0 5 per cent antazoline (Antistine) hydrochloride ophthalmic solution, will give quick relief

Morphine sulfate 8 mg hypodermically may be given to relieve pain and for sedation Alcohol must be avoided Shock and circulatory collapse should be treated by transfusions of plasma or whole blood If hemorrhages appear, transfusions of whole blood, 10 per cent calcium gluconate, 10 cc intravenously, vitamin C, 1 0 gm orally, and vitamin K 10 mg intravenously in 10 per cent dextrose infusion, are indicated Respiratory embarrassment, when present, should be treated by oxygen inhalation, pentamethylenetetrazol (Metrazol), 0 1 to 0 3 gm orally or intravenously, or caffeine sodium benzoate, 0 5 gm subcutaneously or intravenously

If sepsis develops treatment with penicillin streptomycin, or aureomycin should be carried out as described under Bacterial Infections For the prevention of tetanus, the usual prophylactic dose of 1500 to 2000 units of anti tetanic serum should be given Penicillin procaine, 300 000 units in aqueous suspension intramuscularly daily for 3 days, is also advised

Prophylaxis The wearing of leather high-top shoes or leather leggings affords excellent protection Loose heavy trouser legs are of some help and the tropical helmet with its wide brim gives some protection against arboreal snakes In heavily infested areas care should be taken in traveling at night since most snakes are nocturnal in their habits Alertness, careful watch for snakes, and the ability to recognize the warning rattle will prevent many bites

Poisonous Lizards

The gila monster of the southwest United States and the beaded lizard of southwest Mexico are poisonous and their bites must be treated

Frostbite

In this discussion frostbite refers to excessive dry cooling of a portion of the body not to actual freezing There is no unanimity of opinion on proper treatment some advising the rubbing on of snow others recommending rapid heating Probably neither is advisable Gradual warming to room temperature seems best Rubbing and massage should not be used as the resultant trauma to the skin may cause more pain If pain is severe some cooling may be necessary such as the application of ice bags followed by very gradual warming Warm drinks or an alcoholic beverage may be given Concering the latter it should be said that alcohol taken before exposure to cold tends to increase the hazards of cold its use should be limited to the period of treatment for frostbite

Frostbitten extremities should be protected from bed clothing and should be wrapped in sterile dressings covered with several layers of wool Infection should be avoided by careful handling cleanliness and the use of chemotherapy

Unless the freezing is deep gangrene of frostbite is usually superficial similar to ergot gangrene and amputation should not be hasty Recovery is usually rapid although thereafter the frostbitten member is considered to be more susceptible to cold

Prevention The prevention of frostbite is even more important than its treatment It should consist chiefly in the wearing of correct clothing and footwear for protection from exposure The maximum insulation is obtained from loose light many layered clothing Gloves rather than mittens should be worn For the care of the feet dry unwrinkled woolen socks and the avoidance of cracks and abrasions of the skin are important Some advocate the use of an oily application to the feet such as olive oil mineral oil or possibly even lanolin the idea being that a coating of oil increases the phenomenon of supercooling allowing exposure to lower temperatures without freezing A beard can act as a hazard rather than as protection since frosting of it can lead to freezing of the face

Trench Foot and Immersion Foot

These result from over exposure to wet cold The experiences of World War II demonstrated amply that conservative measures produce

circumstances (a) improper return to atmospheric pressure after working under pressure in deep water and (b) rapid ascent into the atmosphere

The treatment will be considered in two categories preventive and curative

The *preventive treatment* in the case of deep sea workers should consist entirely of proper *decompression* This means gradual elevation in steps, to the water surface Details of the time intervals at the various levels of pressure for proper decompression have been tabulated by the U S Navy

Feet	Minutes
100	85
110	75
120	60
130	55
140	45
150	40
1,0	30

The symptoms are usually preventable the error being made by the worker who becomes careless and attempts to surface too rapidly Symptoms do not occur from compression pressures under 18 pounds to the square inch (roughly 40 feet of water) so that divers can work at that level under water for any length of time and may surface rapidly with no apparent risk When the pressure becomes higher the working shifts must be shortened accordingly At 30 to 35 pounds the shift should be no longer than 6 to 8 hours at 45 pounds pressure, 2 to 3 hours, at 50 pounds pressure not over 1 hour At higher pressures than these the exposure should be for only a few minutes at a time

Studies in World War II under the auspices of the National Research Council showed that breathing pure oxygen for half an hour or an hour before descent is extremely useful in preventing decompression sickness

Ordinarily the symptoms of caisson disease will not occur if the decompression — that is the return to normal sea level oxygen pressure — is sufficiently slow This is accomplished by having the worker raised in stages to the various levels of known pressures and remain progressively longer and longer at each stage until the surface is reached The first stages may be fairly rapid the last ones comparatively slow For example a diver working at 140 feet may be raised immediately to

use of hot-water bottles, and so on, with careful checking of the rectal temperature every 10 or 15 minutes With heat stroke the instability of the heat-regulating mechanism of the body may require several days of careful observation and treatment

Ordinarily, morphine and epinephrine should not be used If convulsions occur sodium pentothal intravenously, in a dosage just sufficient to quiet the patient should be given Inhalation anesthesia or lumbar puncture or both also may be helpful under such circumstances

Intravenous infusions should be used very cautiously in heat stroke, for cardiac decompensation may supervene With hemoconcentration and the picture of shock, a transfusion of blood plasma should be given Oxygen should be given if cyanosis develops If pulmonary edema occurs, rapid full phlebotomy is indicated

Heat Exhaustion

In heat exhaustion in which the temperature is often subnormal, the principle therapy should consist of measures to restore body temperature and the use of stimulants to combat shock The patient should rest in a cool quiet place with the head somewhat below the recumbent body level The manifestations of heat exhaustion are frequently the result of excessive loss of chloride from the body this warrants the intravenous administration of physiological saline preferably mixed with 2 to 5 per cent glucose Fluid intake should be encouraged not forced, fluid can be given advantageously as hot drinks Stimulants should be used frequently — e g aromatic spirits of ammonia, as smelling salts or in 4 0 cc doses by mouth caffeine sodium benzoate, 0 5 gm subcutaneously at intervals of 1 to 2 hours, or epinephrine hydrochloride, 0 5 cc of a 1 1000 solution subcutaneously Oxygen is also of value

When severe muscle spasms are present some advocate the use of 2 0 per cent solution of sodium bicarbonate, 500 to 1000 cc given slowly by the intravenous route

Prevention It has become well established, particularly in industries in which workers are subject to excessive heat, blast furances, et cetera, that heat exhaustion and heat cramps may be prevented by the adequate ingestion of fluid and salt The latter may be given as 0 4 to 1 0 per cent solution of sodium chloride in water sweetened to taste or as salt tablets 0 5 to 1 0 gm taken with each drink of water during the day s work

pression may be helpful in relieving muscle cramps Morphine sulfate may be necessary for extreme pains For circulatory collapse caffeine and sodium benzoate 0 5 gm may be given by hypodermic injection at 20 to 30 minute intervals Artificial respiration may be necessary for respiratory failure

A few cautions should be mentioned In some the joint pains or bends may become worse during recompression This may mean that the pressure is being elevated too rapidly and the difficulty can be overcome by slower application of pressure

In the case of a moribund patient or a patient with severe circulatory impairment or with paralysis treatment at a 60 foot level may have to be given for days at a time

Occasionally during decompression and oxygen inhalation symptoms of dizziness nausea muscular twitching blurring of vision tremor, extreme irritability and apprehension appear owing to oxygen poisoning In such instances the patient should be allowed to breathe room air at short intervals

During chamber pressure reduction spontaneous pneumothorax may occur Thoracocentesis in the pressure chamber may be required in order to complete treatment

There are not infrequent errors in both the diagnosis and the treatment of caisson disease Extremity pains due to injury abdominal pains due to appendicitis, and so on may occur either separately or in addition to the caisson symptoms When in doubt recompress

Finally a recurrence of symptoms may be overlooked or neglected Collapse and death can follow An overnight soak at pressures equivalent to those at depths of 30 to 60 feet is most effective for recurrent symptoms

Motion Sickness

In this category car sickness seasickness and occasional sickness from other forms of motion are included Since the symptoms are probably caused by various mechanisms none of which is well understood the treatment is often difficult and is largely symptomatic Treatment and prevention for the various types of motion sickness are similar and agents effective for one are usually effective for the others

The new antihistaminic drug dimenhydrinate (Dramamine) hydrochloride has been found to be very helpful for motion sickness It is

the best results The patient should be confined to bed, and nothing is applied to the skin surface If significant edema is present the legs should be elevated

The early stage of this condition is usually spoken of as the 'hyperemic phase ' in which treatment should be directed toward maintaining vasomotor tone and in keeping the metabolism of the feet and legs at a low level by rest The torso and arms should be kept warm but the legs should be exposed to cool air from an electric fan or from ice bags applied over sterile towels not directly against the skin surface The latter are useful also in relieving the pain, take care however not to cool the parts too much as this may produce more pain The limbs should not be rubbed or massaged After the pain has subsided the extremities should be exposed to moderately cool room air, (68°F) and then warmed gradually Heat should not be applied at any time By the time normal room temperature is tolerated, Buerger exercises may be instituted with considerable benefit In the late stages, also spoken of as the ischemic phase with circulatory insufficiency, leg ulcers or Raynaud s phenomenon vasodilators should be used Benzazoline (Priscoline) 25 to 50 mg 3 or 4 times a day, Dibenzyline, 60 to 120 mg by mouth daily alternate suction and pressure boot, or, possibly, sympathectomy, is advised

Cold Allergy Hyperergy

In isolated instances desensitization to cold by graded frequent, cooling baths may be helpful In most cases such treatment is not very successful A few instances are on record in which considerable benefit was derived from the use of antihistaminic drugs such as diphenhydramine (Benadryl) hydrochloride and tripelennamine (Pyribenzamine) hydrochloride They may be tried in doses of 50 to 100 mg 3 times a day A single dose of an antihistaminic 50 to 100 mg, may be given beneficially an hour before exposure to cold Occasionally the individual may have to abandon a cool or cold climate for one of a higher temperature where his symptoms do not occur

Caisson Disease

Caisson disease known also as the bends,' is a term used in two

Prevention As a general measure of prevention it is wise perhaps for the individual not to be too active physically and to be moderate in eating and drinking Quick movements should be avoided on voyages of any type Alcohol should not be indulged in by the majority of people although a few claim immunity through its use

In addition motion sickness is prevented if the individual is quiet and recumbent with the head only slightly elevated on a small pillow There should be ample fresh air In order to avoid vertigo it is recommended that the eyes either be kept closed or remain fixed on an object in the distance such as the horizon Some prefer remaining in a darkened room In some people motion sickness may be prevented by avoiding the sight of passing objects in others reading may produce motion sickness since the eyes are under even greater strain Movement of the eyes however, is not the only factor in motion sickness for it has been reported that blind persons have suffered on land on sea and in the air

Specific medications for prevention include the same drugs discussed under treatment namely dimenhydrinate (Dramamine) hydrochloride and the members of the atropine and barbital series In addition small doses of bromides 0 3 to 1 0 gm 3 times a day beginning a day or two before the journey are often effectual

With the increased use of airplane travel several additional measures have been found to be useful in the prevention of motion sickness A good night s rest before a flight a stable ventilation and temperature rate in the cabin and an effort on the part of the pilot to avoid turbulent air are important precautionary measures It has also been proved that flight in higher strata in pressurized cabins reduces by two thirds the incidence of air sickness The application of an abdominal binder moderately tight is often effective in prevention

Mountain Sickness

Acute high altitude sickness is discussed under caisson disease

The condition herein referred to is chronic high altitude sickness — the symptoms that develop when one unaccustomed to high altitudes takes up residence at an elevation of 13 000 to 15 000 feet or higher

Since the symptoms are due to decreased oxygen pressure they may be alleviated somewhat by limiting any physical exertion to the least possible amount thus keeping the body s requirements for oxygen at a

a depth of 50 feet, where he waits 10 minutes, then he is raised to a depth of 40 feet for 10 minutes, then he is kept at 30 feet for 20 minutes, at 20 feet for 30 minutes at 10 feet for 35 minutes, then he may be raised to the surface abruptly

In the case of altitude sickness the symptoms may be prevented by the breathing of pure oxygen before an ascent, this has the effect of denitrogenation Altitude sickness does not usually take place under 18 000 feet and occurs most commonly between 25,000 and 35,000 feet It is said that 45 minutes of preoxygenation will postpone the bends to 30,000 feet, 90 minutes to 34 000 feet 3 hours to 37 000 feet, and 5 hours to 40 000 feet A mixture of oxygen and helium will shorten these times, e g 90 minutes of an oxygen helium mixture is equivalent to 5 hours of pure oxygen

It has been thought by some that a high-fat diet predisposes an individual to caisson disease Therefore a low fat diet has been advised as a preventive measure One study from the files of the National Research Council suggests that a high fat diet may increase the severity of 'chokes The diet that most effectively decreased the incidence of the bends or joint pains was one high in carbohydrates Probably an average normal diet is best together with preoxygenation

Obese individuals and persons of older age should not be employed as caisson workers for they are likely to be susceptible to decompression sickness

The essential feature of the *curative treatment* to eliminate, and certainly to ameliorate the symptoms of caisson disease is immediate *recompression*, followed by very slow decompression Caisson workers and deep sea divers should live and sleep near the medical air lock so that it may be readily available in the first few hours after decompression

In most sizable projects such as caisson works and deep sea salvage there are 'medical air locks in which the air pressure may be controlled readily At the first appearance of symptoms the patient should be placed promptly in such a lock and the room pressure elevated quickly to the level at which the individual has been working With this procedure the symptoms subside rapidly After proper recompression the period of decompression may be begun but very slowly for bubbles once formed in the tissues are not easily eliminated It should take no less than 5 hours, sometimes as long as 24 hours for such decompression following recompression

Hot fomentations and massage to the extremities during decom

CHAPTER XXIX

INTOXICATIONS

Ethyl Alcohol

Acute Alcoholism Moderately marked acute alcoholism requires only time to sleep off the debauch but washing out the stomach is advisable when any considerable amount of alcohol has been taken On awakening from an alcoholic debauch it is well to take black coffee and as soon as possible a considerable amount of any non-alcoholic fluid

In deep alcoholic coma the stomach should be thoroughly washed out If there are evidences of collapse the limbs should be rubbed and their position changed frequently In addition to black coffee it is well to give these patients caffeine sodium benzoate intramuscularly in 1 gm doses repeated in 1 hour if coma does not lessen Amphetamine (Benzedrine) sulfate in doses of 20 to 40 mg intravenously repeated 2 or 3 times at 4 hour intervals intramuscularly is also effective as a stimulant Cortisone 150 to 300 mg intramuscularly is helpful If respiration is depressed a mixture of 95 per cent oxygen and 5 per cent carbon di oxide should be inhaled If convulsions occur sodium pentobarbital 0 2 to 0 3 gm intravenously may be used but great care must be taken to avoid toxic effects from the barbital

In violent acute alcoholic mania 8 mg of apomorphine given hypo dermically will produce nausea followed by vomiting and usually a rapid disappearance of manical symptoms Apomorphine is a dangerous depressant and care must be exercised in its use

If a large amount of alcohol has been taken quickly so as to cause a high alcohol content of the blood its oxidation should be attempted by giving intravenously 100 cc of 50 per cent glucose solution with 20 units of regular insulin and 50 or 100 mg of thiamin chloride

In most of the acute alcoholic patients dehydration is to be expected When present it should be corrected promptly by giving 500 to 1000 cc or more of normal saline solution containing 5 to 10 per cent glucose

administered by mouth in doses of 50 to 100 mg every 4 or 5 hours, that is, before meals and at bedtime Dosages as high as 800 mg in 24 hours have been well tolerated but much smaller doses may cause drowsiness If the drug cannot be retained in the stomach, it may be injected into the rectum with 30 cc of physiological saline solution The results of therapy by either route are usually apparent in half an hour to an hour after the administration of the drug and may last from 10 to 18 hours Diphenhydramine (Benadryl) hydrochloride in 50 to 100 mg doses 3 times a day is also useful

The drugs that have been used most in the past have been of the atropine and barbital series These may be administered if the antihistaminics are not available or if they fail to give satisfactory results Of the atropine series scopolamine [hyoscine] hydrochloride, in doses of 0 6 mg at intervals of 4 to 6 hours is useful This is usually combined with sodium amobarbital (Amytal) 0 - gm orally or intramuscularly at 4 hour intervals, or with phenobarbital, 15 to 20 mg orally if it can be retained

Chlorobutanol (Chloretone) 0 3 to 0 6 gm, in tablets or capsules also may be given 3 to 4 times daily with considerable benefit Amphetamine (Benzedrine) sulfate in doses of 5 mg on arising and repeated once or twice during the day has been used with some success

An attempt should be made to maintain adequate hydration by having the patient hold chipped ice in his mouth or take sips of cool water Some persons vomit so violently that they can keep nothing on the stomach, hence they become dehydrated rapidly and develop acidosis In these cases an intravenous infusion of physiological saline solution is most helpful Some advocate fruit juices to keep up the carbohydrate stores and thus prevent acidosis Others advise cold ginger ale or champagne to lessen the nausea Intravenous dextrose 5 per cent solution, may also be helpful

Concerning diet there are many opinions It may be useful to separate the solids from the liquids giving dry food with sufficient salt added to replace the chloride lost by vomiting A few patients crave salty foods this should be encouraged Some believe that seasick patients should continue to eat regularly in spite of vomiting Unless the patient has a craving for unusual food, which should be satisfied if possible it seems best to adhere to simple foods, these should be increased as vomiting ceases Diets high in fats are best avoided The bowels should be kept open but cathartics should not be given

be completely interdicted Most of these patients will need prolonged management as described under Chronic Alcoholism

Chronic Alcoholism The treatment of chronic alcoholism is a very different problem Results are likely to be far from satisfactory because relapses are almost the rule Treatment is a psychiatric problem for which a properly equipped institution is necessary Success will come only for the individual who wishes to be cured who is willing to undergo prolonged treatment and who realizes that for him any drinking will surely lead to relapse For the chronic alcoholic moderation in drinking is an impossibility which he his family and his friends must realize

Treatment usually begins with continuation of free access to alcoholic drink to which he has added a nauseant such as emetine so that for a time at least the patient will lose his craving for drink in the belief that for some reason it is no longer satisfying To this end various formulas are the basis for so called cures One of these is the recently introduced drug tetraethylthiuram disulfide (Antabuse) This drug is given in an initial dose of 0 5 gm 4 times a day followed by 0 5 gm 3 times on the second day and twice on the third day Following this a maintenance dose of 0 25 to 0 75 gm a day is given as determined by the needs of the patient After 4 days of medication the patient is permitted to sample alcohol while under close supervision He then realizes that he cannot consume alcohol while taking Antabuse without developing unpleasant flushing increased pulse rate and blood pressure and nausea and vomiting *He must be thoroughly cautioned about the use of alcohol and understand* that if it is taken unpleasant and possibly dangerous reactions will occur Such cures temporarily effective have rarely been permanent *and speedy relapse usually follows*

The chronic alcoholic should be put under the care of a competent psychiatrist who is interested in this type of patient and his problem The patient and his family should be prepared for prolonged institutional management followed by office consultations and probable return from time to time to institutional regime It is probable that nothing short of this will cure the chronic alcoholic Alcoholics Anonymous is often a great help

Methyl (Wood) Alcohol

As soon as possible after the ingestion of a considerable amount of wood alcohol in any form gastric lavage should be performed and

minimum As the compensatory alterations occur in the body, activity may be gradually increased until finally acclimitization takes place In some individuals, particularly persons with cardiovascular and/or pulmonary disease, acclimitization may never occur For them a return to lower altitudes is necessary As an emergency measure complete bed rest and inhalation of oxygen under pressure afford prompt relief

BIBLIOGRAPHY

Effects of Physical Agents

1 CONN J W The Effects of Heat ' *Oxford Syst Med*, 1947 ii, p 664 (1)
2 TABBOTT J H The Effect of Cold *Oxford Syst Med*, 1948, iv, p 664 (20-1)
3 WHITE J C Vascular and Neurologic Lesions in Survivors of Ship wreck 1 Immersion Foot Syndrome following Exposure to Cold, *N E J Med* 1943 ccxxviii p 211

manganate solution After lavage with this, 50 cc of a 20 per cent suspension of charcoal and 50 cc of a 50 per cent solution of sodium sulfate should be left in the stomach Gastric lavage repeated at intervals formerly in general use is *no longer advised since this has often seemed* a causative factor in producing pulmonary edema and pneumonitis

Respiratory stimulants should be given Hot strong coffee, caffeine and sodium benzoate in a 1 gm dose repeated at ½- to 1 hour intervals are useful for this purpose N allylnormorphine (Nalline) hydrochloride is effective in quickly reversing the respiratory depression of morphine It should be given intravenously in a dose of 5 to 10 mg and repeated as needed to maintain respiration Doses larger than 40 mg at a time should not be exceeded and usually much smaller doses are entirely satisfactory Nikethamide (Coramine) in intravenous doses of 5 to 10 cc of a 25 per cent aqueous solution given slowly and repeated in 10 minutes if needed may also be used Inhalation of oxygen from a cellophane bag or catheter should be tried especially if the patient shows any cyanosis Care must be taken however to prevent respiratory center failure and possible carbon dioxide narcosis by giving oxygen in proper quantities Lack of sufficient oxygen causes respiratory center stimulation but if too much is given this stimulus is lost and respiratory depression results Means for artificial respiration should be at hand when oxygen is being administered Rarely respiration may have to be maintained by mechanical measures such as a pulmotor or other form of respirator Atropine sulfate 0 4 mg subcutaneously should be given once

Circulatory collapse is usually prevented by the measures just described If it does appear plasma transfusions are of value Digitalis compounds should not be given except to patients with cardiac decompensation

If the patient cannot be kept awake by the hot coffee and caffeine the reflexes should be stimulated by inhalation of ammonia smelling salts and possibly by cold ablutions to the skin The method of keeping the patient awake by forcing him to walk has for the most part been abandoned because the physical and circulatory fatigue is detrimental and it is difficult to keep the patient s body warm The frequent and highly fatal pneumonia in acute opium poisoning was very possibly caused by keeping the patient awake by forced exercise Penicillin 300 000 units daily as procaine penicillin in aqueous suspension intramuscularly is recommended as a prophylactic measure against infection

As soon as possible the patient should return to a normal but simple diet rich in carbohydrate and low in fat, containing not less than 70 gm daily of protein and preferably enriched with vitamins, particularly nicotinamide 25 mg and thiamine hydrochloride, 10 mg by mouth 3 times a day

Delirium Tremens The patient with delirium tremens should always be placed in a hospital where constant attendance and moderate restraint are possible Restraint should disturb the patient as little as possible but should be sufficient to prevent body harm It must always be remembered that the activity of the patient with delerium tremens is unpredictable and may be violent with suicide a constant possibility to guard against Prompt and effective sedation is the most important part of treatment This is accomplished most satisfactorily by paraldehyde in oral doses of 15 to 20 cc or in rectal doses of 20 to 25 cc If for some reason paraldehyde cannot be used chloral hydrate in doses of 1 to 2 gm may be substituted or sodium amobarbital (Amytal) may be given by mouth or intravenously in doses of 0 3 to 0 5 gm As soon as sedation is accomplished sedative drugs should be continued in smaller dosages until the patient s psychical and physical restless activity has greatly decreased or disappeared

Whether to stop alcohol intake completely or gradually has been a matter of much discussion in the past each policy having strong support Now, the general consensus seems to be that abrupt, complete interdiction of alcohol intake is the better procedure

Pneumonia and circulatory collapse are the usual causes of death in delerium tremens Both should be prevented by prophylactic measures and treated promptly if they appear Penicillin 300 000 units of penicillin procaine in aqueous suspension intramuscularly daily, is of considerable value prophylactically and if pneumonia develops penicillin should be given as recommended under Pneumonia It should greatly reduce the mortality from complicating pneumonia and lessen the possibility of circulatory collapse The danger of such collapse will also be decreased by prompt and effective sedation and adequate hydration

If there are signs of developing cerebral edema hypertonic glucose should be given magnesium sulfate by mouth is also helpful

After the delerium tremens ends the patient should be built up as rapidly as possible by a nutritious diet with vitamins added To make up a diet that is high in calories and appeals to a patient who at first wishes to eat very little requires a skilled dietitian All alcoholic drinks should

drawal of the bromide To stimulate its excretion from the body 6 to 10 gm of sodium chloride should be administered daily This may be given in the form of bouillon commercial cubes of which contain 2 to 2 5 gm of sodium chloride hence 3 or 4 cups of bouillon daily will provide adequate sodium chloride in addition to the amount in or added to other items of the patient s diet Of course sodium chloride can be given in enteric coated capsules but these are more often causative of *nausea and possibly of vomiting than is sodium chloride given in* bouillon and diet as just described Sufficient fluids should be given to insure a urinary output from 2500 to 3000 cc daily

If shock is present it should be treated as described on page 642 Occasionally patients will exhibit severe mania requiring paraldehyde 15 cc by mouth or 20 to 30 cc dissolved in an equal quantity of olive oil and given by rectum Restraint of the patient should be avoided *Continuous tub baths or cold wet sheet packs are helpful*

Food intake should be kept up if necessary it should be given by tube A high vitamin high calorie diet is recommended since most of these patients are malnourished and have been on a semi deficient diet Constipation should be relieved by enema until the patient has begun to recover and then cascara sagrada 0 3 gm by mouth is satisfactory Niacinamide *0 3 to 0 6 gm by mouth daily* may be helpful.

Prevention Bromide intoxication is more likely to occur in elderly people in those who are debilitated or have some renal impairment and in those who while still taking bromide, become ill develop anorexia nausea vomiting or diarrhea Any condition leading to a decreased intake of sodium chloride or interference with bromide excretion is likely to cause bromidism Bromide should be given with care or discontinued if the factors mentioned above exist

Barbiturates

Acute Intoxication As a preliminary measure to proper management an immediate survey of the patient s condition should be made and a brief chart prepared indicating the status of consciousness respiration blood pressure reflexes including width of pupil and hydration

Patients showing a mild degree of poisoning with little or no fall in blood pressure or only slight depression of respiration may require little or no treatment. Caffeine in the form of strong coffee or caffeine and

repeated several times at short intervals and then twice daily for several days Colonic irrigation with normal saline is also advisable Sodium sulfate in a dose of 15 to 30 gm should be given by stomach tube following the first gastric lavage Bed rest together with a diet as adequate as possible in calories and containing thiamin, nicotinamide, and vitamin K is indicated Repeated lumbar punctures to remove 15 to 20 cc of spinal fluid is also advised Intravenous infusions of 5 per cent glucose containing 15 gm of sodium bicarbonate or lactate per 1000 cc are to be given and repeated at 6-hour intervals to keep the urine at a pH of 7 In severe cases with marked acidosis gastric lavage with 4 per cent sodium bicarbonate and 6 to 8 gm of sodium bicarbonate by mouth every 2 hours is advised in addition to keeping the urine between pH 7 0 and 7 5 If there is delerium, it should be treated as described for ethyl alcohol intoxication If respiration is shallow and if cyanosis appears, oxygen inhalation by the usual methods is indicated If there is evidence of cerebral edema intravenous hypertonic glucose as 50 to 100 cc of a 50 per cent solution should be given in addition to lumbar puncture Cortisone 150 to 300 mg intramuscularly is helpful

In chronic methyl alcohol poisoning optic nerve atrophy is likely to occur This serious development should be watched for by repeated tests of vision including perimetry If it develops the patient should be referred to an ophthalmologist for treatment

Prevention Obviously any drink that might possibly contain wood alcohol should be avoided It is to be remembered that many liquids containing varying amounts of wood alcohol are likely to be drunk by the chronic alcoholic when he is unable to get drink containing ethyl alcohol This is the source of most of the poisonings with methyl alcohol

Opium

Acute Intoxication Treatment should consist of methods of removing the drug from the gastro intestinal tract stimulation of respiration, prevention of circulatory collapse and keeping the patient awake, it should be commenced just as soon as a toxic amount of opium or any of its compounds has been taken into the body by any route

The patient should remain in bed and should be kept warm to prevent chilling of body surfaces Prompt gastric lavage preferably by nasal tube should be instituted using several liters of 1 5000 potassium per

100 mg will be needed After muscle twitching appears or a previously absent reflex reappears sufficient picrotoxin should be administered to maintain this activity

Care should be exercised to avoid a picrotoxin convulsion which may occur if the drug is pushed too vigorously Picrotoxin in amounts just sufficient to maintain the re established reflex or slight muscular twitching should then be given If convulsions should appear and do not subside in 20 to 30 seconds 0 1 gm of sodium amobarbital (Amytal) or sodium pentobarbital (Nembutal) should be given intravenously

A patient exhibiting a falling blood pressure or a dangerously low pressure should receive in addition to intravenous fluids and plasma, phenylephrine (Neosynephrine) hydrochloride 5 to 10 mg intramuscularly or 3 to 5 mg intravenously repeated at 15- to 30-minute intervals as indicated by the patient s response

If unconsciousness is a major factor and the patient is responding well in other ways amphetamine (Benzedrine) sulfate 20 to 40 mg intra muscularly followed by a dose of 10 to 20 mg in one hour if indicated is helpful

Gastric lavage is a dangerous procedure since it can and often does cause aspiration pneumonia It is indicated if the drug has just been in gested but probably is of limited usefulness if 6 to 10 hours have elapsed If gastric lavage is done sodium sulfate 30 gm in solution should be left in the stomach in order to expedite bowel activity and removal of any unabsorbed drug

Chronic Intoxication Mild chronic intoxication requires only withdrawal of the drug for treatment Symptoms may persist however for 3 or 4 weeks More chronic addiction will need psychiatric treatment as in other drug addictions Barbiturates should be withdrawn with care Sudden withdrawal may produce convulsions A step by step withdrawal over a period of 2 weeks is well tolerated

Drug Addiction

The treatment of drug addicts is extremely difficult and all too often only temporarily effective It should not be attempted by the general practitioner but only by the psychiatrist operating in an institution In general treatment consists of gradual reduction or abrupt cessation of the drug to which the patient is addicted and the temporary substitution

Chronic Intoxication The withdrawal of opium is accomplished with little distress to the patient if methadone in a dose of 1 mg for each 4 mg of morphine is carefully substituted for the morphine Then, when the period of morphine withdrawal is over (7 to 10 days), the methadone is discontinued Unfortunately this is only the beginning and the measures described under Drug Addiction must be carried out if there is to be any hope of success Even with the most approved methods a cure rate of only 20 per cent or so results

Cocaine

Acute Intoxication Treatment for acute cocaine poisoning should be that described under Opium except that convulsions, which may appear in cocaine intoxication should be prevented or suppressed by giving sodium pentobarbital (Nembutal) 0 2 to 0 4 gm intravenously, the dose to be repeated as the condition of the patient indicates

Chronic Intoxication Chronic cocaine poisoning should be managed as described for Chronic Opium Poisoning and for Drug Addiction Withdrawal of the cocaine should be prompt and complete, since withdrawal symptoms and collapse do not follow The body functions without their accustomed cocaine stimulation will be depressed for several days If the customary dose has been large withdrawal may be followed by as many as 36 hours of sleep In extreme cases it may be desirable to awaken the patient by a small dose of cocaine in order to give nutrition

For patients who are addicted to both cocaine and opium effective treatment is more difficult than for those addicted to the single drug

Heroin

Both acute and chronic heroin intoxication including addiction is to be treated as described under Opium and Drug Addiction

Bromide

Bromidism usually occurs in the chronic form Whether it is acute or chronic however, treatment should be by prompt and complete with

by mildly antiseptic cleansing solutions followed by protective dressings to prevent secondary infection Acute toxicity from ingestion of the metal should be treated by gastric lavage several times with warm tannic acid or tea solution Egg albumin precipitates the metal and is helpful when ingested and then removed by gastric tube Magnesium oxide is also helpful Dimercaprol (BAL) should be given as described for arsenic poisoning The patient should be kept warm and caffeine sodium benzoate, 0 5 to 1 0 gm given and repeated in 1 hour if necessary Atropine sulfate 0 4 to 1 0 mg subcutaneously and repeated in 4 to 6 hours is helpful in relieving cramps Morphine sulfate 8 mg subcutaneously should be given if needed for pain

Arsenic Poisoning Acute As soon as possible the stomach should be washed out to remove any remaining arsenic The bowels should be emptied by catharsis with sodium sulfate and renal excretion should be promoted by giving fluids in large amounts unless there is evidence of an existing nephritis The patient should be kept warm and fluid plasma and blood transfusions given to avoid collapse Caffeine and sodium benzoate 0 5 to 1 0 gm intramuscularly is useful for respiratory depression If diarrhea and abdominal pain occur the camphorated tincture of opium [paregoric] 2 teaspoonfuls every 3 or 4 hours or morphine sulfate 8 mg hypodermically should be given instead of catharsis Atropine sulfate 0 5 to 1 0 mg subcutaneously helps relieve cramps

If the poisoning is from the gas arsine or hydrogen arsenide oxygen inhalation should be used in addition to the methods just described Anemia is usual and should be treated by immediate blood transfusion and later by iron medication Dimercaprol (BAL) as a 10 per cent solution in oil 3 mg per kilogram of body weight should be given intramuscularly every 4 hours for the first 2 days followed by 4 injections on the 3rd day and 2 daily thereafter for 10 days or until recovery

Chronic The contact with arsenic should be stopped A course of BAL as described for acute cases seems advisable The skin lesions should be treated with a mildly antiseptic ointment Fluid intake should be increased and a nutritious diet containing milk and vitamins including thiamin and nicotinamide should be given If neuritis is present this should have in addition to the preceding measures treatment as described under Chronic Neuritis Iron should be given as ferrous sulfate or ferrous gluconate 0 6 gm 2 or 3 times a day

Beryllium Poisoning In both acute and chronic beryllium poisoning

sodium benzoate 0 5 to 1 0 gm intramuscularly may be given and repeated as necessary to maintain normal respiration

Individuals exhibiting severe degrees of poisoning may have depression of respiration and blood pressure and may be in deep coma Occasionally one of these vital functions will be hit much more severely than the others In these cases in addition to the general procedure specific measures must be directed toward relieving the depressed function Therefore, if the preliminary survey shows severe respiratory depression as is commonly the case the pattern of management should be as follows

Obstruction to breathing should be eliminated promptly by pulling the tongue forward and aspirating any accumulated salivary and bronchial secretion Oxygen should be given if there is any cyanosis, but care should be exercised that it is not given in sufficient amounts to remove respiratory center stimulating action and so lead to further respiratory depression and possible carbon dioxide narcosis When oxygen is used in these cases, means should be at hand to give artificial respiration Mechanical respiration by a suitable apparatus may be needed The use of caffeine as a respiratory stimulant is generally recommended, although some question its efficacy The patient should be kept warm and fluids should be given freely intravenously if not tolerated by mouth Distention should be avoided A cleansing enema and keeping the bladder open are helpful Infusion of human plasma is indicated if circulatory collapse is severe Since pneumonia occurs so frequently 300,000 units of penicillin procaine in aqueous suspension should be given intramuscularly each day as a prophylactic measure

When respiration is moderately depressed and coma is deep and neither condition has responded to caffeine, pentamethylenetetrazol (Metrazol) 3 0 to 6 0 cc of the 10 per cent solution, should be given intravenously and repeated in 30 minutes if there is no response Picrotoxin should be used if coma is deep and persists, if reflexes especially corneal and pupillary are not obtainable if respiration is markedly depressed and if blood pressure continues to drop It may be given intramuscularly in 5 to 10 mg doses every half hour until any one of the previously absent reflexes returns or slight muscular twitching occurs

Picrotoxin can also be given slowly intravenously at the rate of 1 mg per minute, with pauses every few minutes to allow thorough mixing and maximum effect to take place This should be continued until a muscle twitch appears or a reflex reappears This will usually occur after 10 to 20 mg have been given, although sometimes as much as

water and given by mouth 3 or 4 times a day It can be made more palatable by the addition of fruit juice to the solution A milk diet of 1 to 2 quarts daily is indicated at this stage to promote lead storage In addition calcium lactate 6 to 8 gm and/or sodium citrate 6 to 12 gm should be given daily There is accumulating evidence that disodium hydrogen phosphate 1 to 4 gm by mouth daily or 0 3 to 0 6 gm intravenously 3 times a day is effective in treating lead poisoning It is nontoxic and insures lead excretion

After the colic has ended a low calcium diet should be begun This should exclude milk in any form eggs and green vegetables After a week of this diet ammonium chloride should be given in a dose of 1 gm 3 times a day and gradually increased to 6 to 8 gm a day All of this is to accentuate the negative calcium balance and thus liberate lead from the bones It is well to keep the bowels fairly active by saline cathartics These measures should be continued for from 4 to 6 weeks Dimercaprol (BAL) is of no value in the treatment of lead poisoning

Chronic lead poisoning without colic should be treated by the methods described above to liberate the lead from the bones, but the procedure should be more gradual If there is evidence that considerable lead has been recently absorbed the de leading therapy should be preceded by the methods described for depositing lead in the bones i.e. milk diet and calcium lactate and by removal of the lead from the intestinal tract by saline catharsis

The anemia of lead poisoning should be treated as described under Hypochromic Anemia The nerve lesions should be managed as in Chronic Neuritis

Acute lead encephalopathy should be treated in the same way as other forms of encephalitis in addition there should be a milk diet and a saline catharsis to remove any lead present in the bowel After this has been accomplished a gradual de-leading should be commenced by giving a diet free from milk eggs and green vegetables Ammonium chloride should be given after 2 weeks of this diet commencing with a dosage of 1 gm twice a day and slowly increasing to 6 to 8 gm a day

Prevention As far as possible a workman should not have any continued contact with lead thorough washing of hands and a shower after work with change to fresh clothing from the skin out should be enforced Also fresh air should be insured

Magnesium Poisoning The metal magnesium or one of its alloys may be forced into the skin where by its chemical action generation of gas occurs bringing about a so called chemical gas gangrene This must

of a sedative with slight habit-forming propensities The effects of such reduction procedures should be treated symptomatically These patients need to have their body state built up by adequate nutrition with an ample complete diet This is often difficult to accomplish, especially in the early periods of the treatment The dietary regime should have the supervision of a skilled dietitian Supervised physical exercise, commencing very gradually, is an important part of the treatment Various forms of occupational therapy too are to be instituted Most important of all are study and treatment by a competent psychiatrist interested in the problem of the causative factors and its elimination in each drug addict Effective treatment will necessarily take a long time in the institution, with repeated follow-up interviews with the psychiatrist

Metals

Intoxication from metals and their compounds usually has its source in the industrial processes concerned in preparing or using them Besides this source intoxication may arise from accidental ingestion, including mistaken use of insecticides or rodenticides, from misuse of physicians prescriptions from suicidal intent and/or from recognized or unrecognized body contacts For the first group, industrial physicians are chiefly concerned in recognition and prevention while practicing physicians are the ones who must recognize and treat most instances of the other group A discussion of the more common intoxications with metals in this last category will be given in the following sections

In all industrial intoxication with metals prevention is most important, great care must be taken to prevent contact by workmen with any injurious fumes, dusts or solutions This is the chief factor in prevention and must be supervised by the plant physician in conjunction with the plant engineer

Aluminum Aluminum dust from either metallic aluminum or aluminum oxide may cause chronic lung changes On the other hand, such aluminum dust is used in the treatment and prevention of silicosis, which is discussed on page 572 If chronic lung changes do result from inhalation of aluminum dust removal from contact with the dust is probably the only effective therapeutic measure

Antimony The chief toxic result from antimony compounds is a pustular skin lesion, which is best treated after removal of the contact,

should be eliminated completely Dermatoses caused by contact with some of the mercury salts should be treated, after the causative contact has been eliminated by dimercaprol (BAL)

Nickel, Selenium Tellurium, and Vanadium Intoxications In the industrial processing of these metals and some of their compounds vapors that are irritating to the respiratory tract may be formed and may cause acute bronchitis and pneumonitis Treatment is by immediate removal from access to the fumes or volatilized forms followed by oxygen inhalation and treatment as would be applied in any type of acute bronchitis and bronchopneumonia Some of the compounds of these metals cause dermatitis sometimes of a necrotizing ulcerative form which should be treated by removal from contact and soothing mildly antiseptic ointments Deep ulcers may require curetting The metallic taste and garlic' breath resulting from chronic selenium and tellurium exposure may continue a long time after removal from contacts there is no effective therapy for them but chlorophyll by mouth may help some

Silver Poisoning Silver salts may be absorbed and cause a typical pigmentation *argyria* Once formed this pigmentation will be little affected by treatment although local injection of 1 per cent potassium ferrocyanide and 6 per cent sodium thiosultate has been claimed to decrease the pigmentation

Thallium Poisoning The peripheral neuritis from thallium is to be treated by cessation of contact and then by the measures used in treating neuritis

Zinc Poisoning The so called fume fever smelter s shakes brass chills or zinc shakes are caused chiefly some think solely by inhalation of volatilized zinc particles No permanent damage is done and removing the possibility of inhalation is the only treatment necessary Some zinc salts such as zinc chloride cause sloughing burns which are to be treated by removing the necrotic slough and filling the wound with sodium bicarbonate Dressings wet with sodium bicarbonate solution and later soothing antiseptic dressings should be applied Milder skin lesions should be treated with a soothing mildly antiseptic ointment after contact with the offending zinc salt has been eliminated

Carbon Monoxide

The most frequent gas poisoning occurring in civil life is carbon

the pulmonary lesions are to be treated in the way described for acute bronchitis and pneumonia with bed rest and oxygen inhalation during the acute respiratory phase Secondary bacterial infection is to be watched for, and if it occurs, the antibiotic to which the organism is susceptible should be used in effective doses

The contact dermatitis of beryllium should be treated by removing the patient from contact with the metal If indolent ulcers develop they should be curetted to remove the central causative beryllium crystal and then treated with bland antiseptic ointments Corticotropin and cortisone are also useful in giving temporary relief, especially when pulmonary fibrosis is causing serious respiratory difficulty

Cadmium Poisoning Respiratory lesions should be treated as just described for beryllium poisoning Dimercaprol (BAL) should not be used since it brings about deposition of highly toxic amounts of cadmium in the kidneys with resulting severe destruction of renal tissue

Chromium Poisoning Chrome ulcers of the skin, if not deep should be scrubbed with 5 per cent sodium hyposulfite, followed by saline solution to remove any remaining chromium Dressings wet with 5 to 10 per cent solution of sodium citrate or sodium lactate should be applied If this is not effective the base of the ulcers should be curetted thoroughly Despite treatment chrome perforation of the nasal septum may follow the ulceration Surgical procedures may succeed in closing the septal defect

Respiratory tract symptoms, if present, should be treated as described in the section on Beryllium

Gold Poisoning Poisoning from gold preparations, which occurs almost solely following their therapeutic use is to be treated with dimercaprol (BAL) as described for Arsenic Poisoning

Lead Poisoning Acute lead colic This condition can be relieved promptly by 10 cc of a 20 per cent solution of calcium gluconate given intravenously, this may be repeated intramuscularly if colic persists or returns Calcium lactate 6 to 8 gm, daily by mouth should be continued until lead excretion falls to normal After the possibility of an acute surgical condition has been excluded meperidine (Demerol) hydrochloride in 100 mg doses intramuscularly, or morphine sulfate in 8 mg doses subcutaneously should be given for continued pain The bowels should be cleared by cleansing enemas and by magnesium sulfate, 15 to 30 gm given by mouth Sodium citrate can be used instead of calcium gluconate if desired In severe colic it is given as a 2 5 per cent solution 50 cc intravenously followed by 6 0 gm dissolved in 30 cc of

Carbon Bisulfide Poisoning

The treatment of carbon bisulfide poisoning should be expectant and entirely symptomatic In the occasional case with respiratory failure, artificial respiration together with oxygen given as recommended for barbiturate poisoning should be used Although no effective specific treatment is known certain prophylactic measures may be carried out It has been suggested that a diet high in vitamins be adopted by workers in contact with this gas Large doses of vitamins may be added such as thiamine chloride 10 mg 3 or 4 times a day niacinamide 100 mg twice a day riboflavin 5 mg twice a day and pyridoxine 25 mg twice a day

Benzene (Benzol) Poisoning

Under this heading may be included similar substances such as toluene xylene, and other homologues of benzene solvents, and cleaning fluids Although the toxic effects are usually the result of inhalation of the fumes occasionally the liquid may be ingested and cause poisoning In this case the stomach should be washed out thoroughly with 5 per cent sodium bicarbonate solution followed by a cathartic dose of a saturated solution of magnesium sulfate 30 to 60 cc

The remainder of the treatment is similar to that following inhalation For respiratory failure the patient should be given artificial respiration and inhalation of oxygen as recommended for barbiturate poisoning

Since the major effects are on the blood and blood forming organs bed rest and a high caloric high vitamin diet should be instituted Initially repeated transfusion of whole blood are indicated if the anemia is acute or marked These should be followed in most cases by repeated injections of liver extract or vitamin B_{12} since the anemia is often macrocytic and hyperchromic Concentrated liver extract should be used (15 units to 1 cc) in doses of 2 0 cc daily for 3 or 4 days then 1 cc daily for one week then the injections may be gradually decreased to 3 times twice and once a week Vitamin B_{12} in 1 0 cc doses containing 30 micrograms per cc may be given in the same manner and with the same good effect If the hemoglobin content is low ferrous gluconate 0 3 to 0 6 gm should be given 3 times a day Large doses of calcium as calcium lactate or calcium gluconate 1 0 gm by mouth 3 or 4 times a day are also recommended Good results from large doses of ascorbic acid 200 to 400 mg daily intravenously or orally have been reported

be distinguished from bacillary gas gangrene by bacteriological examination This being done, the former should be treated conservatively by sterile wet dressings and rest of the infected part If secondary infection does occur, it should be treated by the antibiotic to which the infecting organism is sensitive

Manganese Poisoning The chronic central nervous system lesions caused by manganese should be treated as described for Paralysis Agitans, which they closely resemble

Mercury Intoxication Acute Acute poisoning, often suicidal, from mercury bichloride or other mercurial salt should be treated immediately by the administration of dimercaprol (BAL) intramuscularly as described in the section on Arsenic except that the first dose should be 5 mg per kilogram of body weight All mercurial should be promptly removed from the stomach Egg albumin from 3 or 4 eggs should be given promptly followed by lavage with a large amount of solution containing 5 per cent sodium bicarbonate and 10 per cent sodium formaldehyde sulfoxylate Since mercury salts are re secreted into the stomach lavage should be repeated at hourly intervals as long as any mercury can be detected in the washings In addition to gastric lavage catharsis with magnesium sulfate should be carried out If as often happens, the urine shows casts, cells and albumin and particularly if there is oliguria or anuria with increase in blood nitrogen treatment should be as described for Acute Toxic Nephritis Now with the use of dimercaprol (BAL) gastric lavage saline catharsis and measures to increase the urine flow formerly the chief procedures for treating acute mercury intoxication need not be so vigorously carried out

The stomatitis and salivation that are so frequently an evidence of mercury intoxication should be treated locally All aline aromatic solution N F 1 part to 2 parts of water as a mouthwash 3 or 4 times a day, is helpful Dimercaprol (BAL) leads to prompt relief of the mouth lesions as well as relief of general toxicity

Supportive measures such as morphine sulfate 8 mg subcutaneously as required to control pain dextrose solution 1000 cc of a 5 per cent solution intravenously and repeated as needed and caffeine sodium benzoate 0 5 gm repeated as needed are recommended

Chronic The stomatitis and salivation should be treated as described above Nervous manifestations including the curious type of tremor can be influenced very little by any therapy Dimenhydrinate (Dramamine), 50 to 100 mg 3 times a day may help Obviously the mercury contact

pentobarbital or thiopental sodium (Pentothal) should be given intravenously slowly in dosage just sufficient to lessen or control the convulsion For muscular twitchings causing severe discomfort 5 per cent magnesium sulfate solution 1 0 cc per 10 pounds of body weight should be given intramuscularly and repeated as needed If the depressant effect of magnesium sulfate becomes too marked it may be counteracted by intravenous calcium chloride or calcium gluconate given slowly Should the recommended atropine fail to relieve adequately the bronchospasm aminophyllin 0 5 gm given slowly intravenously or epinephrine 0 cc of a 1 1000 solution given intramuscularly should be used Great caution is necessary with the latter for it may exaggerate the central effects of these agents

With impending respiratory failure all drug therapy may be ineffective Artificial respiration may then prove to be the only lifesaving procedure and it should be instituted at once The Emerson hip raising method is effective The Shafer prone method is of no value because of muscle paralysis When death occurs it is due to respiratory failure from central depression and peripheral paralysis of the muscles of respiration

The *arsenical blister gases* or vesicants are exemplified by lewisite or chlorovinyldichloroarsine They may cause local or systemic effects from absorption through the skin

Personal decontamination as soon as possible is imperative this may be accomplished by using a protective ointment especially prepared for this purpose or by wiping the skin with sodium hypochlorite solution and alcohol followed by thorough washing with soap and water

For local and systemic poisoning dimercaprol (BAL) is a specific remedy The ointment should be applied freely to the local skin burn and a layer of ointment left in place For systemic treatment it is given as a 10 per cent solution in peanut oil together with 0 per cent benzyl benzoate and is injected intramuscularly The dose should be 3 mg per kilogram of body weight every 4 hours around the clock for the first days 4 injections on the third day then injections daily for another 5 to 10 days or until recovery The armed forces have standardized the dosage of dimercaprol (BAL) as follows for a person of 125 pounds 2 5 cc 150 pounds 3 0 cc 175 pounds 3 5 cc 200 pounds 4 0 cc If pulmonary symptoms or other evidences of severe arsenical poisoning are present the interval between the first and second doses should be shortened to hours

monoxide poisoning, either by accident or with suicidal intent Both the concentration of the gas and the duration of exposure are important in determining the extent of poisoning

In *acute poisoning* the treatment consists of removing the patient from the source maintaining respiration — artifically if necessary, as by the Schafer prone pressure method or the newer Holger-Nielsen Emerson hip lift or Silvester push-pull methods of resuscitation — and the administration of adequate oxygen Oxygen given preferably 'on the spot,' is recommended It has been shown that as much as half of the carbon monoxide can be eliminated from the body during the first hour after exposure with the prompt use of oxygen Carbon dioxide as a 6 per cent mixture with oxygen is frequently used The addition of carbon dioxide commonly leads to deeper and more rapid respirations but this does not add much to carbon monoxide removal and the carbon dioxide can pose an extra hazard if respiratory center failure occurs Administration need not be continued longer than an hour or two If a gas apparatus cannot be obtained quickly at the scene of the accident, the patient should be transported to a hospital being given artificial respiration on route if necessary In addition, the patient should be kept warm with blankets and hot-water bottles Any exertion on the part of the patient should be avoided Artificial respiration and oxygen inhalation may need to be given together A mechanical respirator, such as that used in poliomyelitis may be necessary when normal respiration has failed

Other measures such as venesection with removal of carbon monoxide hemoglobin and transfusion of whole blood to improve the oxygen carrying capacity of the circulation may be tried This procedure, however is not always successful

Methylene blue once advocated for this condition, is now considered to be harmful and should not be used Caffeine as caffeine and sodium benzoate 0 5 gm should be given at frequent intervals as a respiratory stimulant but such drugs as strychnine alpha lobeline epinephrine, morphine digitalis and so forth not only are not indicated but may even be harmful Procaine hydrochloride may be helpful in serious comatose cases A dose of 500 mg in 500 cc of 5 per cent dextrose is given intravenously over a 2 hour period For coma lumbar puncture may be useful In such circumstances fluid and electrolyte balance should be maintained

In case of *chronic poisoning*, the individual should be removed permanently from any contact with carbon monoxide gas

pentobarbital or thiopental sodium (Pentothal) should be given intravenously slowly in dosage just sufficient to lessen or control the convulsion For muscular twitchings causing severe discomfort 25 per cent magnesium sulfate solution 1 0 cc per 10 pounds of body weight should be given intramuscularly and repeated as needed If the depressant effect of magnesium sulfate becomes too marked it may be counteracted by intravenous calcium chloride or calcium gluconate given slowly Should the recommended atropine fail to relieve adequately the bronchospasm aminophyllin 0 5 gm given slowly intravenously, or epinephrine 0 2 cc of a 1 1000 solution given intramuscularly should be used Great caution is necessary with the latter for it may exaggerate the central effects of these agents

With impending respiratory failure all drug therapy may be ineffective Artificial respiration may then prove to be the only lifesaving procedure and it should be instituted at once The Emerson hip raising method is effective The Shafer prone method is of no value because of muscle paralysis When death occurs it is due to respiratory failure from central depression and peripheral paralysis of the muscles of respiration

The *arsenical blister gases* or vesicants are exemplified by lewisite or chlorovinyldichloroarsine They may cause local or systemic effects from absorption through the skin

Personal decontamination as soon as possible is imperative this may be accomplished by using a protective ointment especially prepared for this purpose or by wiping the skin with sodium hypochlorite solution and alcohol followed by thorough washing with soap and water

For local and systemic poisoning dimercaprol (BAL) is a specific remedy The ointment should be applied freely to the local skin burn and a layer of ointment left in place For systemic treatment it is given as a 10 per cent solution in peanut oil together with 20 per cent benzyl benzoate and is injected intramuscularly The dose should be 3 mg per kilogram of body weight every 4 hours around the clock for the first day 4 injections on the third day then injections daily for another 5 to 10 days or until recovery The armed forces have standardized the dosage of dimercaprol (BAL) as follows for a person of 1 5 pounds 2 5 cc 150 pounds 3 0 cc 175 pounds 3 5 cc 200 pounds 4 0 cc If pulmonary symptoms or other evidences of severe arsenical poisoning are present the interval between the first and second doses should be shortened to hours

The prophylactic measures to be used against benzene poisoning include adequate ventilation originating from the floor (benzene fumes are heavier than air), preferably by means of suction, and avoidance of contact with the skin Ordinary rubber gloves do not withstand the action of benzene, synthetic rubber gloves do, and these should be used In addition it is useful to rub olive oil or other animal or vegetable fat into the skin before handling the substance

Obviously employees should be instructed in the dangers and symptoms of benzene poisoning and employers alerted to the appearance of toxic symptoms

War Gases

There are three important classes of war gases (1) simple tear gases, (2) nerve gases or the G series and (3) arsenical blister gases

The *lachrymating gases* cause severe burning and lachrymation of the eyes The more common ones are chloracetone and chloracetophenone They are nuisance agents that ordinarily have no harmful effects on the eyes or mucous membrances Removal from the source of gas should be prompt Weak alkali such as 2 0 per cent sodium bicarbonate solution may be used with benefit to wash the eyes Bandages should not be applied Dark glasses may be worn for photophobia

The *gases of the G series* are the most recent development in the field of chemical warfare They are nerve gases having a physostigmine like action Inhalation of the vapors or liquid contamination of the skin may cause death in a few minutes if the individual is unprotected A gas mask should be applied promptly if possible before exposure begins

The physiological effect of these agents is an irreversible inactivation of cholinesterase This includes pupillary constriction spasm of the ciliary body of the lens of the eye bronchoconstriction, bronchorrhea, increased motor activity of the gastro intestinal tract, and generalized skeletal muscle fibrillary twitchings Headache nausea vomiting, salivation and diarrhea follow

The treatment of poisoning consists chiefly in preventing excessive nervous activity by avoidance of fear physical activity, and any external stimuli Quiet gentle handling is the first essential As soon as possible the patient should be given an antidote of atropine sulfate 1 0 mg, intravenously or intramuscularly For the pupillary constriction with its associated headache 1 0 per cent atropine sulfate solution should be instilled into the conjunctival sac If convulsions occur either sodium

11 LONGCOPE, W T and LUETSCHER J A Jr "Symposium on Medical Therapeutics Treatment of Acute Mercury Bichloride Poisoning with BAL (2 3 dimercaptopropanol)" *Med Clin No Amer* 1950 xxxiv p 469
12 MARGOLIS H M and CAPLAN P S "BAL in Treatment of Toxicity from Gold" *Ann Int Med* 1947 xxvii p 353
13 NYSWANDER M "Withdrawal Treatment of Drug Addiction" *N E J Med* 1950 ccxlii p 126
14 PROCTOR C D and KAHN H S "Disodium Hydrogen Phosphate Therapy in Lead Poisoning" *Am J Med Sc*, 1950 ccxix p 316
15 STRECKER E A "Psychotherapy in Pathological Drinking" *Jour Amer Med Assoc* 1951 cxlvii p 813
16 WHITTENBERGER J L and SARNOFF S J "Physiologic Principles in the Treatment of Respiratory Failure" *Med Clin No Amer*, Sept 1950, p 1335

Dimercaprol in oil may cause severe reactions Tenderness at the site of injection may last for several days Certain systemic symptoms begin usually 15 to 30 minutes after injection and may last for half an hour or longer They may include a feeling of constriction in the throat oppression in the chest mild lachrymation, burning of the lips and dryness of the mouth There may be a transient rise in blood pressure A few patients experience restlessness and nervousness, with sweating of the hands mild nausea and vomiting Unless severe, none of these symptoms contraindicates further use of the drug

BIBLIOGRAPHY

Intoxications

1 AMYES E W RAY J W and BROCKMAN N W Carbon Monoxide Anoxia Intravenous Administration of Procaine Hydrochloride in Treatment of Acute and Chronic Effects *Jour Amer Med Assoc* 1950 CXLII p 1054

2 DALE, P W and EBAUGH F G Antabuse Therapy in Chronic Alcoholism *Am J Med Sc* 1950 CCXX p 103

3 DeFOREST R E and POTTHOFF C J Back Pressure Arm Lift Method for Administering Artificial Respiration Recommended" *Jour Amer Med Assoc* 1951 CXLVII p 1454

4 EAGLE, H MAGNUSEN H Systemic Treatment of 7 Cases of Arsenic Poisoning (Encephalitis Dermatitis Blood Dyscrasias Jaundice Fever) with 3 dimercaptopropanol (BAL) *Am J Syph Gon and Ven Dis*, 1946 xxx p 4 0

5 HAMILTON A and MULTIPLE AUTHORS Industrial Toxicology ' *Oxford Syst Med* 1951 ii p 595

6 HARDY H BISHOP R and MALOOF C Treatment of Lead Poisoning with Sodium Citrate *A M A Arch Indust Hyg*, 1951 iii p 267

7 HARRIS A and DERIAN P Niacinamide (Nicotinamide) in Bromide Intoxication *South Med Jour* 1949 XLII p 973

8 JONES A DOOLY J and MURPHY J Treatment of Choice in Barbiturate Poisoning *Jour Amer Med Assoc*, 1950 CXLIII p 884

9 KEENEY A and MILLINKOFF S Methyl Alcohol Poisoning *Ann Int Med* 1951 XXXIV p 331

10 KLINE, E. INKLEY S and PRITCHARD W Five Cases from Fluorescent Lamp Industry Treatment of Chronic Beryllium Poisoning with ACTH and Cortisone *A M A Arch Indust Hyg*, 1951 iii, p 549

amounts and gradually increased to a full liquid diet then semi solid food may be followed by bland solid food the calorie value being steadily increased

If diarrhea continues 2 teaspoonfuls of the camphorated tincture of opium [paregoric] should be given every hour and then every 2 hours, or better, after each watery bowel movement In all except the intensely severe cases with marked prostration, this drug should be commenced at once Aluminum hydroxide mixed with kaolin (Kaomagma) or pectin (Kaopectin) in doses of 15 to 30 cc at 2- to 3 hour intervals should be begun at the same time

If the causative bacteria have been identified the appropriate antibiotic should be given in the usual dosage and route

Prevention This kind of food poisoning will not occur if cooked foods are not left standing at room temperature open to air contamination and if canned foods are eaten soon after the can is opened and are similarly protected until they are eaten Prompt and continued refrigeration in modern electric or gas refrigerators is a very important preventive measure Since rats and mice sometimes carry the bacteria they should be eliminated from places where food is kept

Akee Poisoning Vomiting Sickness of Jamaica

This is caused by eating fruit of the *Blighia sapida* that has not properly ripened The disease should be treated promptly by emptying the stomach and in adults giving some alcoholic liquid such as brandy or whiskey since alcohol acts as a precipitant of the poison contained in the toxic form of the fruit Supportive measures are helpful Convulsions may require sodium pentobarbital (Nembutal) 0 1 to 0 2 gm intravenously

Botulism

As soon as this poisoning is diagnosed the patient should be given botulism antitoxin after testing for sensitivity either the specific one if the causative type or organism is known or a polyvalent one this is given intravenously in doses of 10 000 to 20 000 units and repeated as indicated by continuing symptoms The antitoxin will be far more

CHAPTER XXX

FOOD POISONING

Bacterial and Viral Poisoning

Bacterial organisms of the salmonella or proteus group, *Staphylococcus aureus*, and less frequently streptococcus of varying types including *S hemolyticus*, *S fecalis*, and *S viridans*, are not uncommonly causative of food poisoning The organisms grow in foods, especially carbohydrate foods that are left standing uncovered without having been cooked or after having been cooked and not properly refrigerated, and then are eaten without having been thoroughly heated Viral organisms, too although for the most part unidentified, are often causative

Treatment should consist of bed rest, keeping the patient warm cessation of food by mouth gastric lavage unless there is frequent vomiting maintenance of a large fluid intake of water by mouth unless nausea and vomiting prevent in which case normal saline may be given subcutaneously or intravenously It is important to give fluid to compensate for fluid loss by vomiting and diarrhea preventing dehydration is one of the chief measures of treatment When there is marked collapse, as is often the case in addition to giving fluid as described and keeping the patient warm in bed the plan of treatment described in the section on Shock should be followed including plasma or blood transfusions Warm applications to the abdomen are comforting and when abdominal cramps tenderness and pain are marked, morphine sulfate, 8 mg combined with atropine sulfate 0 5 mg should be given hypodermically and repeated in 4 hours if needed Some prefer to use meperidine (Demerol) 0 1 gm intramuscularly

Castor oil used often in the past is now given by relatively few physicians As soon as the patient can take any food fruit juices albumen water, hot broths and/or boiled milk should be given in small

Vol VIII 353

Prevention Obviously the best method of prevention is not to eat any grain products contaminated by the ergot fungus *Cla iceps purpurea* or tal e ergot containing drugs in toxic amounts

Favism

Favism is caused by ingestion of the raw or cooked beans of the plant *Vicia faba* or by inhalation of the blossoms The induced acute or chronic hemolytic anemia, with its hemoglobinuria should be treated by removing from the gastro-intestinal tract any remaining products of the bean by lavage and catharsis by stopping access to the blossoms and by transfusion if the anemia is very marked or by iron, as described for Chronic Hemolytic Anemia if the anemia is moderate All possible contact with the plant should be avoided after recovery since there appears to be an allergic factor present Epinephrine (Adrenalin) hydrochloride 0 3 to 0 5 cc of a 1 1000 solution subcutaneously, is helpful in combating allergic symptoms which usually consist of respiratory difficulty and vascular collapse Antihistaminics may also be useful. Corticotropin 100 mg intramuscularly or cortisone, 100 to 150 mg by mouth may prove most helpful

Lathyrism Lupinosis Vetch or Chicken pea Poisoning

The powdered grains of certain vetches chiefly *Lathyrus sati us* and *L cicera*, are sometimes mixed with meal made from other cereals and are used to make bread They may cause a spastic paralysis mainly of the legs, but sometimes complete paraplegia Treatment should be similar to that recommended for other forms of spastic paralysis Neostigmine (Prostigmine) methyl sulfate, 1 0 cc of a 1 2000 solution subcutaneously repeated at 3 or 4 hour intervals for the first day or two followed by neostigmine (Prostigmine) bromide 15 mg by mouth every 4 hours for the next 2 or 3 days is very helpful

Milk Sickness

In addition to gastro-intestinal disturbances from pathogenic and saprophytic bacteria growing in improperly handled milk man may

effective if given in the first 24 hours of botulism, it may be used later on, but probably will give less and less benefit The stomach should be thoroughly washed out with a nasal tube, a purgative given — either castor oil or magnesium sulfate — and the colon irrigated Water and other fluids should be given freely by nasal tube, and soon a soft solid, later a solid nutritious diet should be given if the patient can swallow with ease If there is respiratory difficulty, as is usual, a respirator should be used if one is not available artificial respiration should be given Oxygen should be given also, particularly if any cyanosis appears Caffeine sodium benzoate 0 5 gm intramuscularly, repeated as the patient's condition indicates, is helpful Severe respiratory failure may respond to picrotoxin given intravenously as a 1 1000 solution in a dose of 1 cc per minute until respiratory depression is relieved or there is a return of pupillary corneal or slight muscular reflexes but care must be taken to avoid convulsions In all of the treatment the patient should be managed so that a minimum of exertion is necessary on his part since fatigue is likely to induce or accentuate muscle paralysis

Prevention Any canned or other food should be discarded if it seems softer than it should be contains gas bubbles, or has a cheesy or rancid odor Danger comes chiefly from home packed jars of vegetables It is well to boil all such vegetables before tasting, even if there are no evidences of spoilage, since sometimes seemingly perfectly good cans will contain botulinus toxin boiling for 10 to 15 minutes will destroy any toxin that may be present

Ergotism

This may be either acute or chronic Acute ergotism should be treated by gastric and colonic lavage and magnesium sulfate catharsis, plus the usual treatment for shock if that occurs Chronic ergotism can cause gangrene of the fingers toes ears and nose and a variety of nervous manifestations which are to be treated symptomatically as described for the diseases of the nervous system in which these symptoms appear The gangrene should be treated as gangrene from frostbite Vasodilator drugs are helpful and should be tried Papaverine hydrochloride, 30 to 60 mg subcutaneously 4 to 6 times a day, benzazoline (Priscoline) hydrochloride 25 to 50 mg by mouth or subcutaneously 4 to 6 times a day, or Dibenzyline 60 to 120 mg by mouth daily, is helpful in relieving vascular spasm

sulfate, 60 cc of a 50 per cent solution A 2 per cent solution of sodium bicarbonate should be used for washing out the stomach 500 cc of this to be left in the stomach Respiratory failure which is not uncommon should be treated by artificial respiration or, better by the use of a respirator and oxygen inhalations should be given Treatment to prevent shock and collapse should be instituted

Prevention As the poisoning is caused by a flagellate organism on which the mussel feeds mussels should not be eaten in the summer months when this flagellate abounds especially when it is in sufficient abundance to color the sea water red rust color, as not infrequently happens If there is any doubt about whether the mussel is poisoned it should be avoided the white meat may be eaten but only after it has been thoroughly washed and boiled for 30 minutes in water made highly alkaline with sodium bicarbonate

Partridge Poisoning

Severe collapse nausea, vomiting and diarrhea are sometimes caused by eating grouse or so called partridge that have fed on a poisonous berry Treatment should be as described for Bacterial and Viral Poisoning

Potato Poisoning

Sometimes sprouting potatoes develop an increased amount of solanine a poisonous principle that if present and eaten in sufficient amount may cause chills fever headache vomiting diarrhea colic and great prostration The poisoning is treated by thorough gastric lavage and 30 gm of magnesium sulfate dissolved in water is left in the stomach to empty the intestinal tract Treatment to prevent shock and collapse should be instituted

Prevention Potatoes that have lain partly exposed above ground during growth or that have become well sprouted owing to poor storage should not be eaten.

develop a disease similar to that called "trembles" in cattle, from drinking milk from cows that have fed on either snake root or rayless golden rod, in man, this disease is sometimes called "the slows" Treatment is symptomatic If acidosis develops, the stomach should be washed out with a solution of sodium bicarbonate part of which is to be left in the stomach The incident weakness calls for prolonged bed rest

Mushroom Poisoning

The stomach should be emptied promptly, either by stomach tube or by induced vomiting The former is preferable, with magnesium sulfate, 60 cc of a 50 per cent solution being used and some of the solution being left in the stomach to promote catharsis Colonic irrigation is advisable In *A muscaria* poisoning, atropine sulfate in large subcutaneous doses is specific A dose of 2 mg should be given promptly and repeated at intervals until it causes moderate toxic effects, it is an antidote to the toxic principle muscarine Dextrose in 5 to 10 per cent solution in normal saline solution should be given intravenously in 500 cc amounts and repeated frequently to promote diuresis If there is evidence of blood destruction, and this occurs with mushrooms that contain hemolytic toxin blood transfusions in amounts to counteract this are indicated Corticotropin 75 to 100 mg, or cortisone, 200 to 300 mg intramuscularly, may be beneficial If restlessness or excitement becomes serious morphine sulfate 8 mg subcutaneously, is helpful Adequate relief for severe excitement may require phenobarbital, 0 1 to 0 2 gm by mouth or sodium pentobarbital (Nembutal), 0 1 to 0 2 gm dissolved in 10 cc of normal saline and given intravenously The vomiting diarrhea abdominal colic and collapse that are often caused by the eating of mushrooms are to be treated as described under Bacterial and Viral Poisoning

Prevention No wild mushrooms should be eaten unless the gatherer is entirely familiar with the poisonous varieties, especially *Amanita phalloides*, *A muscaria*, *A verna*, and *Helvella esculenta*, and is careful not to pick them

Mussel Poisoning

After the stomach has been washed out thoroughly with warm normal saline, the intestines should be emptied by catharsis with magnesium

PART XI

AVITAMINOSES

CHAPTER XXXI

DEFICIENCY DISEASES

Nutritional knowledge has advanced rapidly in recent years and laboratory information based on experiments on small animals has been an important factor in this advance. Unfortunately the gap between clinical observation and animal experiment has left much room for speculation; unwarranted claims for therapeutic measures have been all too common. In the opinion of the authors a conservative approach to this problem is the wiser course and the one that in the end will place the treatment of deficiency diseases on a sounder basis. Therefore only the definitely proved deficiency states will be discussed here.

Most deficiency states are not the result of an inadequate amount of any single factor but rather are the result of a lack of several essential substances. As a consequence treatment must be so organized as to insure adequate intake and utilization of all essential substances. There are at present 14 clinically recognized diseases known to be the result of inadequate intake or improper utilization of dietary factors.

Adequate dietary intake of carbohydrate, fat, minerals, proteins and vitamins, if properly utilized, will prevent any of these states. Such a diet for the average individual consists of approximately 3000 calories a day containing, besides fat and carbohydrate, not less than 1.0 gm of protein per kilogram of body weight, vitamin A 5000 units, thiamine hydrochloride 2 mg, nicotinamide [niacinamide] 20 mg, riboflavin 3 mg, ascorbic acid [vitamin C] 75 mg, vitamin D 400 to 800 units and adequate amounts of minerals, especially calcium and iron. Approximately 1.0 gm of calcium and 15 mg of iron will supply the daily needs. An adequate diet can be selected from the following commonly recommended dietary pattern:

Feedings should be given 6 or 7 times a day It is desirable to give extra feedings in the form of eggnogs prepared by beating one egg in 8 ounces of milk adding sugar and vanilla to taste and sprinkling with a dash of nutmeg if that is liked Occasionally it will be necessary to give soft or even liquid diets in the beginning of treatment of severe deficiency states Where liquid diets are indicated eggnogs ice cream creamed soups and cereal gruels are excellent Soft diets are essentially the same as liquid diets except that soft cooked eggs mashed potatoes soft puddings and custards have been added

When the deficiency state is marked the diet should be supplemented by the addition of concentrated or purified vitamins If the deficiency is mainly of the vitamin B complex dried yeast powder U S P 4 to 6 ounces daily made palatable by mixing it with tomato juice may be given Liver also may be given orally either as the liquid extract in a dose of 60 to 90 cc or as powder extract in a dose of 15 to 30 gm daily Since yeast and liver extracts are unpalatable to many and as there are often associated deficiencies in vitamin C and occasionally in vitamins A and D purified vitamins in approximately the amounts shown below given 1 to 3 times a day depending on the needs of the individual are excellent supplements to the diet

Folic acid	10 mg
Thiamine	5 mg
Nicotinamide	50 mg
Riboflavin	5 mg
Ascorbic acid	75 mg

When indicated either vitamin A 5000 to 25 000 units or vitamin D 1 000 to 10 000 units daily or both may be added When there is evidence of greater deficiency of any one vitamin that vitamin should be given in extra amounts either orally or parenterally

The treatment of known specific deficiency states varies with the cause and the lesions produced Therefore this treatment will be discussed under individual headings

Vitamin A

Deficient intake of vitamin A leads to hemeralopia (day blindness) nyctalopia (night blindness), hyperkeratosis (phynodermia) keratomalacia and xerophthalmia

Fruits and fruit juices one or more servings daily Select fruits high in vitamin C, such as oranges tomatoes and grapefruit.
Meats eggs cheese and fish one to two servings daily
Vegetables 2 or more servings daily Include spinach, carrots (for vitamin A) salads consisting of cabbage, lettuce tomatoes (for vitamin C) in addition to the usual vegetables such as potatoes beans peas et cetera
Breads and cereals especially whole grain ones for iron phosphorous protein thiamine and nicotinic acid
Fat and butter supplying fat and vitamin A Oleomargarine, if enriched with vitamin A is also satisfactory
Milk one pint to one quart daily depending on age Young growing children should have at least one quart a day, adults require less one pint being sufficient

When dietary deficiency exists or is suspected because of alcoholism associated with disease inadequate food intake, dietary irregularities or unusual dietary requirements the diet must be more than adequate and must be supplemented by concentrated or pure dietary essentials Such a diet for the treatment of dietary deficiency should supply 3000 to 4000 calories with 120 to 150 gm of protein and abundant amounts of minerals and essential food factors Careful consideration must be given to the desires habits and food pattern of the patient if the maximum degree of benefit is to be obtained All too often impractical menus, loaded with strange or disliked food lead to failure in therapy When the patient co operates in selecting the diet he is more apt to eat it The following diet is a good example of the general type satisfactory in treating deficiency states

Fruit juice one glass daily Select orange tomato, or grapefruit juice
Cereal one large serving daily Select oatmeal, cream of wheat wheatena or shredded wheat
Bread 2 slices with each meal toasted when desired
Meat lean meats chicken fish or cheese 6 ounces daily
Eggs 4 daily May be used in eggnogs, et cetera
Vegetables potatoes carrots beans peas turnips beets rice cabbage parsnips lettuce beet greens spinach, et cetera, 4 servings daily
Fats butter or oleomargarine with added vitamin A, 6 pats daily
Ice cream 3 servings daily
Milk at least one quart daily

Healing is slow but all ocular lesions will usually disappear in 2 months leaving a variable degree of residual damage

Prevention An adequate diet containing milk butter carrots peas green beans squash and greens will prevent vitamin A deficiency Where there is diarrhea sprue or other abnormality of the gastro-intestinal tract leading to a loss of the vitamin parenteral administration must be used in order to maintain adequate amounts of the vitamin An intake of 5000 to 6000 units in children and 3000 to 5000 units in adults will prevent symptoms of deficiency

Vitamin B Complex

Deficiency in this complex leads to ariboflavinosis beriberi pellagra, and sprue Several other conditions that are less well defined are most likely due to inadequate amounts of the vitamins in this complex

Ariboflavinosis Treatment consists in placing the patient on an adequate diet supplemented by the purified vitamin formula In the usual case riboflavin 10 to 15 mg divided into 5 daily doses and given orally is satisfactory Occasionally it is necessary to give the vitamin in an intramuscular dose of 5 mg twice daily for best result Rarely is a larger dose indicated There is definite advantage in giving the dosage in divided amounts since when large amounts are given at one time, much of it is excreted in the urine The eyes should be shielded from light to guard against photophobia If there is intense itching and burning of the eyes boric acid washes may prove helpful Immediate relief from these symptoms may sometimes be secured by the application of a drop of 0 5 per cent ophthalmic antazoline (Antistine) hydrochloride solution or 2 5 per cent suspension of cortisone into the eye The skin lesions of cheilosis may be softened by applying lanolin or if there are indications of secondary bacterial invasion an antibiotic ointment effective against the organism is indicated

Prevention A daily intake of 2 mg of riboflavin for children and 3 mg for adults if properly absorbed and utilized will prevent the development of the various lesions of ariboflavinosis An adequate diet containing eggs meat milk whole wheat and green vegetables will prevent the development of this deficiency

Thiamine Deficiency Inadequate intake improper absorption or abnormal utilization of thiamine may produce one or several of the symptoms of beriberi such as peripheral polyneuritis paralysis edema

Hemeralopia and *nyctalopia* respond slowly to treatment The patient should be placed on an adequate diet rich in vitamin A A dose of 10 000 to 25 000 units of vitamin A daily is recommended Cod liver oil or carotene in oil is less expensive and is satisfactory For those who do not like the taste, however a concentrated form in capsules, such as oleovitamin A may be used In patients with chronic diarrhea or sprue, or in cases where the vitamin is lost by absorption on such agents as aluminum hydroxide it may be necessary to administer it intramuscularly At first a dose of 1 0 cc containing 50,000 units is recommended on alternate days This may be reduced later to 50,000 units twice a week and finally to 50 000 units once a week until oral administration can be resumed or until the lesions have healed Patients should be cautioned about the delay in dark adaption, especially in regards to driving an automobile at night

Hyperkeratosis, like hemeralopia, responds slowly to treatment A dose of 50 000 to 100 000 units of vitamin A daily is recommended Usually the skin becomes moist and soft and perspiration returns in from 2 to 3 weeks The hyperkeratotic lesions, however, may take as long as 4 or 5 months to heal, and scars often remain at the sites of the lesions Where oral medication is unsatisfactory, intramuscular dosage as described under hemeralopia should be given If there is associated infection sulfonamides penicillin streptomycin, or other antibiotic, as indicated by the nature of the infection should be given

Keratomalacia and Xerophthalmia These conditions are serious and require prompt vigorous treatment The patient must be placed on an adequate diet, rich in vitamin A and containing such foods as milk, butter, carrots squash greens and green beans Vitamin A, 10 000 to 25,000 units daily should be started at once and continued until definite evidence of healing is present The dose is then reduced to 10 000 units a day until healing is complete If necessary, intramuscular therapy, as described under hemeralopia is recommended Associated infections are treated with the appropriate antibacterial agents If local infection is present in the eye the pupil should be kept dilated with atropine sulfate in order to prevent adhesions Atropine however, should not be used in the presence of glaucoma One drop of a 1 per cent solution of atropine sulfate daily usually suffices Local applications of a penicillin solution containing 500 units per cc every 2 or 3 hours, or ophthalmic ointments containing aureomycin or terramycin will prove most helpful if the invading organism is sensitive to any of these antibiotics

butter or broth plus nicotinamide 100 mg to be reduced to 50 mg and then to 25 mg as improvement occurs As signs of deficiency disappear yeast and the supplementary vitamins may be decreased

Patients with pellagra should be in bed protected from sunlight and under constant supervision if there are mental symptoms Dry sterile dressings on the skin usually suffice for skin lesions If secondary infection is present appropriate antibacterial therapy should be given Anemia if severe may require blood transfusion As the gastro intestinal tract returns to normal additional iron as ferrous gluconate 1 to 2 gm should be given daily until the anemia is ameliorated The diarrhea responds rapidly to specific therapy but occasionally in the first few days of treatment the use of tincture of opium 2 0 cc every 4 hours will prove helpful Phenobarbital in mild sedative doses may be required to lessen mental agitation and nausea Stomatitis requires gentle mouth care Toothbrushes which may further damage the injured mucous membrane and irritating or spiced foods should be avoided Frequent rinses with the alkaline aromatic solution—N F diluted 1 to 3 times with water as a mouthwash is helpful

After recovery the patient must be informed about the nature of his disease and instructed carefully concerning the dietary requirements necessary to avoid a relapse

Prevention Education regarding the nature of the disease and the inclusion of milk lean meats eggs and fresh vegetables in the daily diet will prevent pellagra In endemic areas and especially among people in the lower economic levels the widespread use of powdered yeast will prevent the disease from developing This is particularly true in the spring when the body supply of nicotinic acid is near exhaustion Better sanitation wiser selection of food and better living conditions all lead to less pellagra The alcoholic until his habit can be cured must be placed on an adequate diet and should receive supplemental yeast powder or niacinamide until his own stores are replenished

Sprue Treatment for sprue should commence with complete bed rest It is essential that fatigue emotional excitement and tension either mental or physical be avoided Dietary treatment is exceedingly important and with the help of the patient a palatable diet high in protein low in fats and polysaccharides such as starch but high in monosaccharides such as glucose should be arranged It should consist mainly of protein Lean meats such as beef lamb liver fish and chicken cooked rare and eggs milk cheese and fresh fruit are excellent and should be

or cardiac enlargement and failure The patient should be placed either on an adequate diet supplemented by brewers' yeast, 90 to 120 gm, 3 times a day in tomato juice peanut butter, or broth, or on purified vitamins Thiamine chloride should be given orally in a dose of 10 mg 3 times a day for mild cases For severe cases 20 to 25 mg 2 to 4 times a day may be given If necessary thiamine may be given intramuscularly In very ill patients and those with cardiac failure 50 mg may be given intravenously 2 or 3 times a day until mouth dosage can be resumed Patients with cardiac failure must be treated by bed rest, digitalis diuretics, and salt restriction as described under Cardiac Decompensation This form of heart failure responds slowly, and prolonged rest is essential It may be months before recovery is complete As a rule neurological disturbances and edema subside more readily Since there is usually an associated deficiency in other vitamins, especially of the B complex, they should be given in 5 to 10 times the usual daily requirement

Prevention An adequate diet containing fresh pork, liver, ham, beans, peas oatmeal and enriched bread will usually prevent deficiencies of this type In the presence of diabetes mellitus, hyperthyroidism infections, anorexia or vomiting the diet must be supplemented by thiamine chloride given either orally or parenterally, if deficiencies are to be prevented The usual daily requirement of 2 mg of thiamine chloride in the diet is insufficient in such conditions, and a supplementary amount should be given to insure a total daily intake of 3 to 4 mg

Pellagra An insufficiency of nicotinic acid in the body results in the lesions of pellagra Severely ill patients should receive an immediate intravenous infusion of physiological saline solution containing 5 per cent dextrose, 100 mg nicotinamide 100 mg thiamine chloride, 50 mg riboflavin, 50 mg pyridoxine 20 mg folic acid and 200 mg ascorbic acid During the first few days of treatment and until therapy by mouth can be started, this infusion should be given 3 times a day Sufficient physiological saline should be given to correct dehydration

As soon as food can be taken by mouth the regular liquid diet supplemented either by brewers yeast, 30 to 60 gm 3 times a day in tomato juice, plus nicotinamide 100 mg twice a day after meals, is to be given As recovery progresses the diet is to be changed to a soft one and then to a normal high calorie, high vitamin diet containing meat, eggs, fresh vegetables milk and fruit, this is to be supplemented by 30 to 60 gm of brewers' yeast 3 times a day in tomato juice peanut

extract is also curative and the crude aqueous extract may be given intramuscularly in a dose of 5 0 cc daily

Since the inability to absorb fats properly and the diarrhea lead to a loss of fats fat soluble vitamins calcium iron protein and other dietary constituents various pathological states develop Chief among these are malnutrition tetany hemorrhages anemia and neuritis These must be anticipated prevented when possible and treated when found to be present The diet already advised may be enriched by adding concentrated protein hydrolysate 30 to 90 gm given daily when indicated Dicalcium phosphate or calcium lactate 3 to 4 gm also should be given daily If evidences of calcium deficiency appear calcium should be given intravenously as 10 per cent calcium chloride or calcium gluconate in a slowly administered daily dose of 10 cc until all symptoms disappear and the blood calcium is normal If calcium loss is marked or if signs of tetany appear the dose should be increased to 20 cc and repeated as symptoms demand Dihydrotachysterol (Hytakerol) 2 5 to 12 5 mg should be given daily for a few days until the tetany is controlled and the blood calcium approaches normal The dose should then be reduced to 1 or 2 doses weekly of 1 25 to 5 5 mg Care must be exercised to avoid too large a dosage A positive urinary Sulkowitch test or elevated blood calcium indicates toxic dosage Viosterol or Drisdol 00 drops or a vitamin D capsule containing 50 000 I U should be given daily as blood calcium becomes normal this may be reduced to the supplementary level of 10 000 units Occasionally because of poor gastro intestinal absorption it is necessary to give vitamin D intramuscularly When intramuscular administration is required 600 000 units of a sterile solution of vitamin D is to be given

Hemorrhages resulting from a lack of vitamin K which is poorly absorbed in sprue are treated by giving vitamin K, menadione sodium bisulfite subcutaneously intramuscularly or intravenously 4 mg daily until the prothrombin time becomes normal The dose may then be reduced to that required to keep the prothrombin level normal

Macrocytic anemia of sprue responds promptly to liver or folic acid therapy but the secondary anemia from hemorrhages and lack of iron requires supplementary iron and when severe transfusions Iron as ferrous gluconate which is preferable or as ferrous sulfate should be given as soon as the condition of the gastro intestinal tract permits A dose of 1 to 2 gm daily after meals is adequate

If recurrences are to be avoided these patients must be instructed

provided Fatty and starchy foods, such as butter, cream, oily salad dressings, pastries potatoes beans, corn, bread, cereal and candies, should be avoided as far as possible The following diet will suffice in the usual case

Breakfast	Skimmed milk 1 large glass
	Fresh fruit banana or scraped raw apple, large serving
	Eggs preferably soft boiled not fried
	Toast 1 slice
10 00 a m	Eggnog eggs in large glass of skimmed milk prepared to taste with dextrose and desired flavoring
Noon	Skimmed milk 1 glass
	Meat large serving chosen from those listed above
	Vegetables peas squash spinach lettuce, cabbage 2 servings of each or 1 serving plus a salad
	Crackers and cheese
4 00 p m	Eggnog as at 10 00 a m
	Fresh fruit banana or apple, may be substituted for the afternoon eggnog
Dinner	Tomato juice or fruit cocktail either fresh or canned
	Broth beef or chicken
	Meat large serving
	Vegetables 2 servings avoid starchy ones
	Gelatine dessert containing fresh fruit
	Skimmed milk large glass
8 00 p m	Eggnog as at 10 00 a m

Where there are severe gastro-intestinal disturbances, nausea vomiting, and diarrhea a bland semi liquid diet or a liquid diet consisting of *skimmed milk* banana powder and purified protein hydrolysates may be required before more solid food can be administered In very severe cases, until food can be retained by mouth it may be necessary to give all food by vein in the form of physiological saline solution to which has been added 10 per cent dextrose 5 per cent purified protein hydrolysate and the essential *vitamins*

Specific therapy in the form of folic acid, 10 mg orally or intramuscularly 3 times a day should be started promptly Brewers yeast, if tolerated, 60 gm daily in tomato juice is an excellent dietary supplement If yeast is not well tolerated purified vitamin, in approximately 2 to 5 times the normal requirement, should be given twice a day Liver

dissolved in 500 cc of physiological salt solution) and slowly injected intravenously Care must be taken to avoid extravasation of the solution into surrounding tissue since it is exceedingly irritating and may produce tissue necrosis If desired ascorbic acid neutralized with sodium bicarbonate may be given *intramuscularly as a 10 per cent solution*

Patients with scurvy often have an associated deficiency of other essential vitamins The diet therefore should be supplemented by purified *vitamins in 2 to 5 times the normal requirements until all deficiencies are* controlled

Patients who show hemorrhagic tendencies should be in bed Careful instruction should be given to prevent any trauma to joints or other areas of the body which might precipitate a hemorrhage The mouth should be rinsed out several times daily with the mild warm alkaline aromatic solution—N F diluted 1 to 3 Occasionally the stomatitis is made worse by secondary infections If infection is present antibacterial therapy with aureomycin troches may be helpful If the infection does not clear promptly oral or parenteral therapy with an antibiotic effective against the organism should be given in adequate dosage

Constipation may be relieved by an enema and definite effort should be made to avoid straining at the stool Where painful hemorrhages exist as in joints splints analgesics and occasionally aspiration are indicated

Prevention A diet supplying from 30 to 150 mg of ascorbic acid depending on whether the individual is an infant who requires 30 mg or a pregnant woman who requires 150 mg will prevent ascorbic acid deficiency The average adult requires about 75 mg of ascorbic acid daily This amount is normally supplied by a diet rich in green vegetables and fresh fruits especially fruit juices such as orange grapefruit or tomato juice It should be borne in mind that cooking oxidizes much of this vitamin

Vitamin D

Deficiency of vitamin D leads to rickets in infants osteomalacia in adults and tetany in both age groups

The treatment of rickets consists of ultraviolet irradiation or of the oral or intramuscular administration of vitamin D Ultraviolet light irradiation *however is satisfactory only for the treatment of mild cases* Vitamin D as cod liver oil halibut liver oil percomorph oil synthetic

about the nature of their disease and must remain on a high calorie, high vitamin diet with a daily intake of at least 10 mg of folic acid

Prevention Adequate dietary intake of meat, milk, eggs, and fresh fruits will be preventive If patients with early symptoms of the disease are treated promptly with the high-calorie high-vitamin, low fat diet adequately supplemented with dried brewers' yeast powder, intramuscular or intravenous liver or folic acid, 5 to 10 mg daily, they will respond readily and further development of symptoms will be prevented The case treated early usually does not become severe but tends to run a benign course with much less tendency to recurrence

Vitamin C

Deficiency of ascorbic acid causes a loss in intercellular substance with consequent inadequate connective tissue support capillary fragility, and hemorrhagic tendency When severe this condition produces the disease known as scurvy

Treatment consists of the prompt administration of a diet rich in ascorbic acid Fruit juices such as orange tomato pineapple, grapefruit and lime are excellent sources of ascorbic acid Cabbage, lettuce tomatoes potatoes cantaloupe turnips green peppers strawberries bananas peaches lemons oranges and apples also are excellent sources of this vitamin Cooking destroys much of the ascorbic acid content of some foods and consequently fresh or raw fruits and vegetables are more effective than cooked ones

In mild uncomplicated cases dietary treatment alone is usually sufficient to bring about a prompt remission of symptoms The daily diet should include 8 to 10 ounces of fruit juice 2 servings of vegetables rich in ascorbic acid meat and one quart of milk

Patients with moderate deficiency should receive in addition to a diet rich in ascorbic acid 0 2 to 0 3 gm ascorbic acid daily by mouth This dose should be maintained until all symptoms have cleared and the blood ascorbic acid level is normal

Severe cases with painful stomatitis or massive hemorrhages should be given sodium ascorbate 0 3 to 0 6 gm intravenously or intramuscularly daily until healing begins Then sodium ascorbate or ascorbic acid should be given by mouth in the same dosage until all symptoms have disappeared and the blood level is normal If ascorbic acid is given parenterally it should be well diluted with physiological saline (0 3 gm

drops, percomorph oil 5 to 10 drops synthetic oleovitamin D (Viosterol in oil) 5 drops or calciferol (Drisdol in propylene glycol) 2 to 3 drops Exposure to sunlight or ultraviolet light until a considerable area of the body is tanned is also helpful Premature infants and people with dark skins such as Negroes and southern Europeans, may require 2 to 3 times the usual prophylactic dose Pregnant and nursing mothers should receive at least 800 I U daily for their own protection Where children cannot receive adequate supervision, a single dose of 600 000 I U by mouth or intramuscularly will protect them for approximately 3 months Milk fortified with vitamin D by the addition of vitamin D concentrate by irradiation or by feeding of irradiated yeast to cattle is protective in normal full term infants but for absolute protection it is wise to supplement it with approximately one half the usual daily prophylactic dose

Vitamin K

Inadequate levels of vitamin K leading to hypoprothrombinemia are not common but may occur as a result of inadequate intake and faulty absorption In newborn infants inadequate stores and intake are the *important factors while in older children and adults faulty absorption* such as occurs in biliary obstruction celiac disease severe diarrhea and sprue is more likely to be the predominating factor Repeated measurements of the prothrombin deficiency resulting from lack of vitamin K indicate the severity of deficiency and subsequent response to treatment Once the diagnosis of vitamin K deficiency is made treatment consists of administering vitamin K menadione in a dose of 1 to 2 mg daily for periods up to 4 weeks In the presence of biliary obstruction 2 to 4 gm of bile salts should be given with each dose of menadione to insure maximum absorption Patients unable to take the vitamin by mouth should be given *menadione sodium bisulfite dissolved in physiological* saline intramuscularly subcutaneously or intravenously in a dose of 2 to 4 mg this should be repeated in 12 hours and then once daily until the prothrombin time is normal Leukopenia may occur in patients receiving excessive *or long continued administration of menadione*

Prevention Diets that include tomatoes spinach and other green vegetables supply adequate amounts of vitamin K Hemorrhagic disease of the newborn resulting from vitamin K deficiency can be prevented by the administration of 1 to 4 mg of menadione sodium bisulfite in-

oleovitamin D, or calciferol, must be used in more serious cases Cod liver oil although widely used, is unpalatable to many, is bulky, and, in small infants can be hazardous owing to aspiration with consequent lung damage An added disadvantage is that large quantities must be given when it is employed as a prophylactic agent or in the treatment of mild rickets In severe rickets excessive doses may be necessary to supply amounts of the vitamin In view of these facts, synthetic oleovitamin D and calciferol have the advantage in that both are highly effective and when given in small amounts, will supply the needs of even the most severe rachitic case

Patients with mild rickets respond rapidly to a daily oral dose of vitamin D that supplies 1600 to 2000 I U This is contained in 8 to 10 drops of percomorph oil 12 to 14 drops of cod liver oil concentrate and 6 to 8 drops of calciferol (Drisdol) or synthetic oleovitamin D Moderate to severe cases require 5000 to 10 000 I U of vitamin D daily This is supplied by a daily oral dose of percomorph oil 25 to 50 drops cod liver oil concentrate 35 to 70 drops or calciferol (Drisdol) or synthetic oleovitamin D (Viosterol in oil) 20 to 40 drops Serial x ray studies of bones should be made and as improvement and healing occur the dose may be gradually reduced to prophylactic levels

Severe refractory rickets and osteomalacia cases should receive 10,000 to 50 000 I U daily These requirements are supplied by 50 to 250 drops of percomorph oil 70 to 350 drops of cod liver oil concentrate or 40 to 200 drops of synthetic oleovitamin D (Viosterol) or calciferol (Drisdol) all given daily by mouth If it is more desirable the requirement can also be supplied by giving one capsule of calciferol (Drisdol concentrated solution in oil) containing 50 000 I U vitamin D daily *Osteomalacia cases should receive* in addition to adequate vitamin D *therapy a high calcium intake* A diet containing at least 2 gm of calcium daily *should be prescribed* In addition calcium lactate 4 to 6 gm daily should be given by mouth for 1 week, the dose may then be reduced to 2 to 4 gm and continued for 2 more weeks

Patients who do not absorb vitamin D properly from the gastro-intestinal tract should be given sterilized vitamin D by intramuscular injection

Tetany developing as a complication of rickets should be treated as described under Tetany

Prevention In ordinary circumstances a daily intake of at least 600 to 800 I U of vitamin D should be maintained *This may be secured by* a daily dose of cod liver oil, 4 to 8 cc cod liver oil concentrate, 5 to 10

PART XII

DISTURBANCES IN METABOLISM

CHAPTER XXVII

DISTURBANCES OF CARBOHYDRATE METABOLISM

Diabetes Mellitus

The aims in the treatment of diabetes mellitus are (1) to keep the urine as free from glucose as possible (2) to maintain a body weight within average limits for the age height and sex of the individual (3) to prevent complicating infections coma and in pregnancy stillbirths and thus (4) to attempt to make the life of the diabetic as nearly normal happy and gainful as possible

Depending upon the circumstances under which the diagnosis is made and the severity of the disease treatment may require hospitalization or in the milder uncomplicated cases it may be carried out in the office with the patient living at home. Single blood or urine glucose determinations are no index of the severity of diabetes mellitus In the case suspected of being only mildly or moderately severe it is frequently useful to perform a glucose tolerance test as a guide to future therapy In the advanced diabetic this is neither necessary nor desirable for it is not needed for diagnosis and may temporarily at least increase the difficulties of treatment

The following outline gives the principles of treatment that should be used in most circumstances with suggestions for office procedures as well as for hospital routine In either event a complete history and physical examination is necessary in order to detect among other ab

tramuscularly to the mother during the last few hours before delivery Administration of menadione 1 mg orally, to the newborn infant is also very effective Patients with sprue, celiac disease, severe diarrhea, or biliary obstruction, and occasionally those on gastro intestinal absorbants who show decreased prothrombin, should be given menadione sodium bisulfite prophylactically in a daily parenteral dose of 2 to 4 mg until prothrombin time is normal The dose should then be reduced to a daily maintenance dose of 2 0 mg and continued until the patient has recovered

Vitamin P

As yet no definite clinical syndrome has been associated with vitamin P deficiency It is thought by some that a lack of the vitamin leads to decreased capillary resistance Capillary permeability may be measured by the Rumpel Leeds test or the modified Hecht test Response to therapy should likewise be determined by these tests

Capillary abnormalities thought to be due to vitamin P deficiency may respond to Hesperidin methyl chalcone 10 to 20 mg orally 3 times a day or to Rutin 20 to 40 mg orally 3 or 4 times daily For the most part results with vitamin P preparations are not striking and many observers are of the opinion that it is valueless Recent studies indicate that certain preparations of vitamin P may have anti-sterility action in man when taken orally

the home as well as in the hospital After control of glycosuria has been attained tests twice daily morning and evening and later even once a day or every other day will be sufficient particularly when long acting insulins are being used With regular insulin the optimum plan is a test of the urine before each meal until regulation of the patient s regime has been obtained after regulation once or better twice daily is sufficient

Diet The most important part of the treatment of diabetes next to use of insulin is the diet Its chief function is to help in the control of the glycosuria thereby maintaining the blood level of glucose in an optimum range Next in importance is a proper division of foodstuffs to maintain an optimal body economy a balance based on optimal weight as derived from actuarial statistics In children this must allow sufficient calories for growth In the adult on the other hand it usually requires a reduction in calorie intake since the majority of adult diabetics are overweight The reduction of obesity in diabetic adults serves still another purpose in that weight loss of itself often improves glucose tolerance and thereby aids materially in the control of the disease The thin diabetic on the other hand should be given a calorie intake large enough to lead to a body weight that is optimal for age height and sex

The average physician treating diabetes is mentally hampered if he is required to carry in his pockets all sorts of tables and charts to guide him The following rules concerning weight and diet are easily re membered and applicable

Average Weight Without having to consult tables of age height and sex each time the physician should be able to estimate quickly ap proximately what his patient should weigh in order to calculate more easily the required diet *In adult females* between the ages of 18 and 50 the weight should be 105 pounds for 5 feet in height plus 5 pounds for each additional inch Thus a female of 5 feet and 4 inches should weigh about 125 pounds In *adult males* the same formula obtains with an extra 10 pounds added Thus for a male of 5 feet and 10 inches in height the weight should be 155 pounds plus 10 pounds a total of 165 pounds *In children* from birth through puberty the rule for average weight is the age times 5 plus 17 Hence an average child of 8 years should weigh approximately 57 pounds Because of tremendous variations in growth rate through puberty between 12 to 18 years of age a little interpolation is required in rules for weight just given

Plan of Diet The planning of the diet for individual patients may be carried out in either of two ways One may attempt to control the

normalities any obvious or hidden local infection, especially of the urinary tract, or pulmonary tuberculosis, both of which as long as they remain active, can nullify the best attempts to control the diabetes

Since the patient's behavior particularly in eating plays such an important role in the control of his diabetes, it is of the utmost importance to explain very early the nature of his condition and the substantial part he must play in its treatment He not only must have an understanding of why the carbohydrates must be regulated in his diet but also must know how to test his urine accurately for glucose and — always an enigma to the new diabetic — how to balance his diet Certain food values therefore must be memorized by him so that he can make accurate substitutions in his diet to prevent monotony and inadequate control of his diabetes All of this should not be attempted in the first few days lest the patient become overwhelmed by the seemingly great complications of directions being given him, but should be accomplished gradually

Urine Test This can be carried out by the Benedict qualitative reagent over a flame or in a hot-water bath, or by the more simple and convenient Clinitest It should be pointed our however, that the latter is not as sensitive as the former, when the clinitest is negative it does not mean that no glucose is being spilled in the urine A word of caution should be given also about heating in the Benedict test if the heating is prolonged (more than 2 minutes of boiling over a flame or more than 5 minutes in a boiling-water bath) urinary phosphates (yellow) may be precipitated, which when shaken into suspension will give a green reaction that may be read as 1 plus sugar when no sugar is present

In the beginning the urine should be tested for glucose 4 times a day before each of the main meals and at bedtime In the hospital this may be done in fractional collections from 7 to 11 a m from 11 to 4 p m from 4 to 9 p m and from 9 p m to 7 a m With either single or fractional specimens a record must be kept of the color reaction as a rough quantitative test of glucose and as a guide to insulin dosage Frequent determinations of fasting blood glucose, although they may be desirable are not necessary and certainly increase the annoyance and the cost of the illness Blood glucose determinations are helpful, however when the diabetes is not well under control When the condition is well regulated blood tests at monthly or bimonthly intervals usually suffice but even without these good management is possible Tests for glucose in the urine however must be kept up regularly in

After computing the total daily calorie requirement the next step is to determine the protein carbohydrate and fat distribution in the diet For the average adult 1 0 to 1 5 gm of protein should be given per day per kilogram of body weight For the growing child 2 0 or even 3 0 gm per kilogram of body weight should be given For the man or woman weighing 70 kilograms 70 to 100 gm of protein per day will be required This would make up 280 to 400 (70 or 100 × 4) of the total daily calories In the case of the growing child of 10 years it may be necessary to give 90 gm protein (67 pounds divided by 2 2 = 30 kilograms 30 × 3 = 90)

On the basis of palatability and calorie content the average diet should contain 65 to 110 gm of fat per day Such a quantity would make up between 585 and 990 calories of the total diet The remainder of the day s diet is to be made up of carbohydrate

Example 175 pound male = 80 kilograms
80 × 1 0 gm of protein = 320 calories (80 × 4)
100 0 gm of fat = 900 calories (100 × 9)

1220 calories

Total daily calorie requirement (80 × 25) = 2000 calories − 12 0 calories = 780 calories to be supplied from carbohydrate 780 divided by 4 = 195 gm for carbohydrate

Although such a distribution of food elements has been stated as desirable for optimal nutrition an initial quantity of 195 gm of carbohydrate in the beginning of treatment of a diabetic may not desugarize the patient satisfactorily It may be tried or one may begin with 150 or 165 gm and as the condition becomes controlled and the tolerance improves increase the carbohydrates to 180 to 200 gm. per day

Some physicians prefer to use a standard form of diet as calculated for a mild moderate or severe diabetic rather than to calculate an outline for the individual patient This is not as desirable as the method already outlined for it fits the patient to the diet rather than *adapting the diet to the patient For those wishing to follow such a plan,* however three such diets are appended (see diets 2 3 and 4)

Distribution of Quantity When the 24 hour requirement of the patient has been calculated a proper distribution of quantity should be made Some prefer dividing the total quantity of foodstuff equally ⅓

diabetes by a calculated diet and by using only enough insulin to control the glycosuria, or one may allow the patient to eat whatever he wishes, the insulin dosage being determined by the glycosuria The former is the better plan for it produces optimal control, maintains the best health, and begins the discipline so necessary in the successful, continued care of the diabetic

Quantitative Prescription of the Diet Fairly rigid quantitative control of the diet is the keystone to successful therapy in diabetes whether insulin is used or not Dietary irregularities invariably lead to imbalance and to the complications that may follow Although emphasis is placed on the carbohydrate moiety in diabetes in beginning the quantitative calculation first consideration should be given to the protein content of the diet because of its importance in maintaining nitrogen balance The remaining carbohydrates and fats are then adjusted in order to "desugarize" the patient, to make the diet palatable and yet to maintain adequate calories for proper nutrition and health In such calculations proper consideration needs to be given to the factor of growth in children and to such associated conditions as renal disease diarrhea, pregnancy lactation disturbances of thyroid function and undernutrition, if any of these are present

For the average otherwise healthy adult the ideal weight as already discussed is converted from pounds to kilograms by dividing by [illegible] From that the daily calorie requirement is calculated according to the sex age, and activity of the individual A very active adult male (laborer) should have 35 to 40 calories per kilogram of body weight per day one doing light work 30 calories per kilogram per day and one with a sedentary occupation or an adult female 25 calories per kilogram of body weight per day Thus an adult male whose ideal weight is 154 pounds 70 kilograms should have 2800 calories (70 x 40) for ordinary labor, 2100 calories (70 x 30) for light work, and at least 1750 calories (70 x 25) for ordinary activity For the growing child 40 to 50 calories per kilogram per day should be prescribed

In the obese patient these calorie valuations should be considerably less than those obtained from the daily food habits of the individual, the subsequent weight loss in itself will usually improve the diabetes In the case of the underweight patient more calories are required In the presence of hyperthyroidism pregnancy infection and diarrhea more calories must be allowed particularly of protein in hypothyroidism and with decreased renal function fewer calories should be given

come tied to his scales, for this detracts greatly from the psychological aim of leading as nearly a normal life as possible

Following are tables of food equivalents (food value in protein carbohydrate, and fat for purposes of substitution) that are quite accurate and yet are simple for the patient to memorize and to supply In Table IX are 6 lists of simplified food equivalents used at the Peter Bent Brigham Hospital These include most of the common foods that furnish in their respective groups approximately the same amount of protein, carbohydrate and fat

List 1 of Table IX gives the protein equivalents of foods that have approximately the same composition as 1 ounce of meat In list 2 are grouped the raw vegetables that may be eaten in more or less unlimited quantity The vegetables of highest carbohydrate content such as *legumes corn, and potatoes,* are included in the equivalents with bread and cereals in list 5 The remainder of the vegetables are grouped together in list 3 and a serving of these vegetables or half a cup is figured as 7 0 gm of carbohydrates and 2 0 gm of protein Since fresh fruits vary considerably in their carbohydrate composition for uniformity the servings of fruits in list 4 are converted into amounts that yield approximately 10 gm of carbohydrate List 5 consists of the carbohydrate equivalents These foods have the same composition as one slice of baker s bread that has a value of 15 gm of carbohydrate and 2 gm of protein *Fat equivalents are given in list 6 and are equal to 1 teaspoonful* of butter containing 4 gm of fat Since the composition of milk differs considerably from that of other foods it is placed in a separate category Furthermore as milk supplies many of the essential nutrients to the diet it is considered basic in the diet and should be included each day

Table X summarizes the carbohydrate protein and fat content of the various food equivalents listed in Table IX Diet number 1, appended, is an example of such a diet calculated for a man weighing 70 kilograms

TABLE IX

FOOD EQUIVALENTS

List 1 Protein Equivalents — Negligible Carbohydrate
7 gm Protein 5 gm Fat 75 Calories

Meat fish poultry — 1 oz	Sardines — 3 medium
Egg — 1	Salmon tuna crabmeat — ½ cup
Cheese American — 1 oz	Peanut butter — 1½ tbs
Cheese cottage — 2 tbs	Cold meat — 3 thin slices
Oysters clams shrimp — 5	Frankfurter — 1 average size

for breakfast, 1/3 for luncheon, and 1/3 for dinner Others prescribe 1/ 7/, and 2/7 Such a decision will depend largely on two factors—the foods habits of the individual and the results of frequent qualitative tests of the urine for glucose If the patient on a 1/3, 1/3, 1/3 division spills the largest amount of sugar in the 7 to 11 a m specimen, a lighter breakfast, such as with a 1/, 2/5, and 2/5 division, will often correct it. Likewise, if a patient on the latter regime is spilling most of the glucose in the 4 to 9 p m specimen, division of the 3 meals into equal parts may help

Another important detail in keeping with the principle of meticulous attention to insure the best success in treatment is consideration of the mealtime In hospitals meals are often served at 8 a m 11 30 a m, and 4 30 p m allowing 15 hours between the evening meal and breakfast A more even time schedule of diet alone or of diet and insulin mav make the difference between success and failure in control of the diabetes A better arrangement is breakfast at 7 30, luncheon at 1, and dinner at 6 30, with perhaps a bedtime snack at 10 For such a schedule the meal division may be 20 per cent 30 per cent 40 per cent, and 10 per cent.

Qualitative Prescription of the Diet This is the most difficult part of the treatment of diabetes particularly for the patient, for it involves a terminology that up to now has usually been a foreign language to the newly diabetic individual Grams calories, and equivalents mav be an enigma at first but they must be understood for proper dietary control of the disease It is best to begin with a calm leisurely discussion of these things so that the patient does not become frightened and overwhelmed As doctors in their student days did not learn about it all in one day, neither should the patient be expected to do so

In the qualitative prescription the physican must keep in mind individual food habits which may be racial social, economic, or religious, the essential nutrients required (minerals and vitamins), and the importance of variety in the menu

The question of the use of scales for weighing foodstuffs requires consideration Their use is highly desirable but not mandatory Scales are one more factor in the teaching of discipline, as well as being the best guide to the amount of food to be served It has been said paradoxically that the best way to avoid the use of the scales is to use them faithfully With them patients soon learn to estimate the gram equivalents of foods much more accurately and easier and better control of the diabetes is the result At the same time the patient should not be-

TABLE X

SUMMARY OF COMPOSITION OF FOOD EQUIVALENT GROUPS

Foods and Equivalents	*Carbohydrate*	*Protein*	*Fat*
Milk — cup	12	8	10
Protein equivalents — list 1	0	7	5
Vegetables — list 2	∞	0	0
Vegetables — list 3	7	2	0
Fruits — list 4	10	0	0
Carbohydrate equivalent — list 5	16	3	0
Fat equivalents — list 6	0	0	4

By the use of Table X it is possible to calculate diet prescriptions with considerable ease and simplicity and to take into account the amounts of each food group the patient is desirous of eating. Nutritive adequacy of the diet is usually assured by seeing that at least one item from each of these food groups is included in the diet and by selecting a variety of vegetables and fruits in order to supply daily one serving of a green or yellow vegetable and one of a fruit or vegetable that is a good source of ascorbic acid.

Variety in the diet is achieved by making use of food equivalents. To facilitate further variety in the diet Table XI is given outlining groups of foods with their equivalents for substitution.

TABLE XI

A LIST OF SUBSTITUTES

The Approximate Carbohydrate Percentage of Fruits and Vegetables

1 to 5 per cent

Asparagus fresh or canned
Beans green wax fresh or canned
Beans scarlet runner
Beans snap
Beet greens
Beets canned
Blackberry juice
Broccoli
Cabbage
Cauliflower
Celery
Chard
Chives
Collards
Cucumbers
Dandelion greens
Dock
Eggplant
Endive
Fennel
Kohlrabi
Lamb's quarters
Leeks
Lettuce
Mung bean sprouts
Muskmelon including cantaloupe and honeydew
Mustard greens
Okra
Okra canned
Peppers green or red
Pumpkin
Radishes
Rhubarb
Romaine
Sauerkraut fresh or canned
Sorrel
Spinach
Squash summer
Squash winter
Strawberries
Strawberry juice
Tomato pureed canned
Tomato juice fresh or canned
Tomatoes fresh or canned
Turnip tops
Turnips
Watermelon
Watercress

List 2 Vegetables — Neglible Carbohydrate, Protein, and Fat

Celery Cucumber Lettuce Radishes

List 3 Vegetable — 7 gm Carbohydrate 2 gm Protein, Negligible Fat (serving ½ cup) 36 Calories

Asparagus
Beans string
Beets
Broccoli
Cabbage
Carrots
Greens beet
chard dandelion
kale mustard
spinach
turnip
Onions
Squash
Tomatoes

List 4 Fruits — 10 gm Carbohydrate, Negligible Protein and Negligible Fat 40 Calories

Apple — ½ medium
Applesauce unsweetened — ½ cup scant
Banana — ½ small
Berries raspberries blueberries or blackberries — 1 cup
Cantaloupe — ¼ medium
Cherries — 12 small
Dates — 2 small
Grapefruit — ½ medium
Grapefruit juice unsweetened — ½ cup
Grapes — 15 medium
Orange — 1 medium or ½ cup juice
Peach — 1 medium
Pear — ½ large
Pineapple fresh diced — ½ cup
Pineapple juice unsweetened — ⅓ cup
Plums — 2 medium
Prunes — 2 medium
Strawberries — 12 large
Tangerine — 1 large
Watermelon — 1 small slice weighing with rind ⅓ lbs

List 5 Carbohydrate Equivalents — 15 gm Carbohydrate, 2 gm Protein Negligible Fat 70 Calories

(Equivalent, 1 slice bread)

Beans baked or lima — ¼ cup
Bread baker's — 1 slice
Corn — ½ cup (1 small ear)
Rice macaroni noodles — ½ cup
Graham crackers — 2
Soda crackers — 5
Pears — 2 cup scant
Potato white — 1 small (size 5 to 1 lb 454 gm)
Cereals cooked — ½ cup
Cereals dry flakes — 1 cup

List 6 Fat Equivalents — Negligible Carbohydrate Negligible Protein, 4 gm Fat 40 Calories

Butter or fortified oleomargarine — 1 tsp
Cream, light — 2 tbs
Mayonnaise — 1 tsp
Oil — 1 tsp
Bacon — 1 slice long crisp
Milk (1 cup 8 oz) — 12 gm carbohydrate 8 gm protein 10 gm fat

Supper

As for dinner

Bedtime

Milk — 1 cup (½ pint)
1 carbohydrate equivalent

Diet No 2 For Mild Diabetes

Diet Prescription Carbohydrate 250 Protein 95 Fat 75, Calories 2000

Breakfast

One 10 fruit — ½ cup or juice of 10% fruit — ½ cup
Bread — 2 slices whole wheat or white toasted if desired
Butter — teaspoonfuls
Cereal — ¾ cup cooked or 1¼ cups ready prepared
Whole or homogenized milk — 1 cup (½ pint)
Egg — 1 prepared any way but fried
Tea or coffee no sugar

Dinner

Lean meat fish chicken or cheese — large serving (2½ oz.), or 2 large eggs or cottage cheese — 6 tbs
One 20 / vegetable — ½ cup
One 15 vegetable — ½ cup
One 15 / fruit — ½ cup
(or any combination of fruits and vegetables equal to 55%)
Bread — 2 slices
Butter — 1½ tsp
Whole or homogenized milk — 1 cup (½ pint)
Tea or coffee no sugar

Supper

As for dinner

Note All measurements given are for the standard 8 oz measuring cup

Clear soups broth (fat free) bouillon cubes mayonnaise made with mineral oil instead of salad oil clear tea and coffee vinegar and saccharine or cyclamate (Sucaryl) may be used in the diet in unlimited amounts

One slice of bread is equal to ½ cup of a 15 / vegetable or fruit

10 per cent

Apple juice
Apricots
Artichokes globe or French
Beans lima canned
Beets
Blackberries
Brussels sprouts
Carrots
Cherries sour
Cranberries
Grapefruit
Grapefruit juice
Lemon juice
Lemons
Lime juice
Limes
Loganberry juice
Onions
Orange juice
Oranges
Peach juice
Peaches
Peas canned
Peas very young
Pineapple
Pineapple juice fresh
Plums (excluding prunes)
Raspberries
Raspberry juice
Rutabagas
Tangerines

15 per cent

Apples
Blueberries
Blueberry juice
Corn green very young
Grapes
Loganberries
Nectarines
Parsnips
Pears
Peas medium
Salsify

20 per cent

Beans baked
Beans red kidney cooked
Cherries cooked
Corn canned
Crabapples
Figs
Grape juice unsweetened
Potatoes
Prunes
Succotash canned

DIET NO 1 SAMPLE OF DIET FOR MAN OF 70 KILOGRAMS OF BODY WEIGHT

Diet Prescription Carbohydrate 50 Protein 115, Fat 100, Calories 2360

Breakfast

1 serving fruit
3 carbohydrate equivalents
3 fat equivalents
2 protein equivalents
Milk — 1 cup (½ pint)

Dinner

3 protein equivalents
Vegetable (list II) — as desired
Vegetable (list III) — 2 servings
3 carbohydrate equivalents
2 fat equivalents
Fruit — 1 serving
Milk — 1 cup (½ pint)

Diet No. 4 For Severe Diabetes

Diet Prescription Carbohydrate 150 Protein 90 Fat 65
Calories 1500

Breakfast

One 10% fruit — ½ cup or juice of 10% fruit — ½ cup
Bread — 1 slice whole wheat or white toasted if desired
Butter — 1 tsp
Whole or homogenized milk — 1 cup (½ pint)
Egg — 1 cooked any way but fried
Tea or coffee no sugar

Dinner

Lean meat fish cheese or chicken — large serving (3 oz.),
or cottage cheese — ½ cup
(1 egg may be substituted for each ounce of meat)
One 0 vegetable — 1½ cup
One 5 vegetable — ½ cup
One 10 fruit — ½ cup
} or any combination of fruits and vegetables equal to 35%
Bread — 1 slice
Butter — 1 tsp
Whole or homogenized milk — 1 cup (½ pint)
Tea or coffee no sugar

Supper

As for dinner

Note All measurements given are for the standard 8 oz measuring cup

Clear soups broth (fat free) bouillon cubes mayonnaise made with mineral oil instead of salad oil clear tea and coffee vinegar and saccharine or cyclamate (Sucaryl) may be used in the diet in unlimited amounts

One slice of bread is equal to ½ cup of a 15% vegetable or fruit

The dietary treatment of diabetes is not complete with prescription of the diet formula as just outlined for even with the best calculations a certain trial and error method must be carried out in each individual

Diet No. 3 For Moderate Diabetes

Diet Prescription Carbohydrate 200, Protein 90 Fat 75
Calories 1800

Breakfast

One 10% fruit — ½ cup, or juice of 10% fruit — ½ cup
Bread — 1 slice whole wheat or white, toasted if desired
Butter — 1½ tsp
Cereal — ¾ cup cooked or 1¼ cups ready prepared
Whole or homogenized milk — 1 cup (½ pint)
Egg — 1 cooked any way but fried
Tea or coffee no sugar

Dinner

Lean meat fish chicken or cheese — large serving (2 oz),
or cottage cheese — 6 tbs
(1 egg may be substituted for each ounce of meat)
One 20% vegetable — ½ cup } or any combination of fruits
One 15% vegetable — ½ cup } and vegetables equal to 45%
One 10% fruit — ½ cup
Bread — 1½ slices
Butter — 2 tsp
Whole or homogenized milk — 1 cup (½ pint)
Tea or coffee no sugar

Supper

As for dinner

Note All measurements given are for the standard 8 oz. measuring cup

Clear soups broth (fat free) bouillon cubes, mayonnaise made with mineral oil instead of salad oil clear tea and coffee vinegar and saccharine or cyclamate (Sucaryl) may be used in the diet in unlimited amounts

One slice of bread is equal to ½ cup of a 15% vegetable or fruit

Regular and crystalline insulin have two major disadvantages the frequent injections required and the uncontrolled nocturnal hyper glycemia and glycosuria that often develop

The dose of each injection should be regulated according to the degree of glycosuria Usually it is most convenient to use insulin containing 40 units per cc unless the dose needed is smaller or larger than the usual requirement In this case insulin containing 20 units 80 units or 100 units per cc may be more satisfactory When insulin containing 40 units per cc is used 8 units are given if the urine shows 1 plus sugar and the dose is increased by 4 units for each plus of increase in sugar in the urine If more than 20 units per injection are required to keep the urine relatively sugar free the diet should be altered to correct this

Occasionally with the regular or ordinary insulin local or generalized allergic reactions may occur This is rare with crystalline zinc insulin Such reactions are due to the fact that ordinary insulin contains small amounts of protein that are not removed during preparation and to which the individual has or may develop sensitivity Such reactions may be avoided by changing either to insulin made from an animal to whose protein the patient has no sensitivity or to crystalline zinc insulin A mixture of pork and beef insulin recrystallized several times has been found to be less allergenic than either alone In a number of cases allergic hypersensitiveness will disappear in the course of time even if the same insulin continues to be used

Protamine Zinc Insulin This is a suspension of a relatively insoluble precipitated compound of insulin zinc and protamine the latter a simple protein obtained from the sperm of certain species of fish This compound has been introduced for use as a long acting insulin because of its slow sustained though somewhat irregular, absorption after sub cutaneous injection Each injected dose forms a subcutaneous depot releasing its insulin at varying rates depending upon size of the dose location of the injection and the individual patient It should be injected at the same time each morning

Its greatest asset is its long action 24 to 30 hours which allows for giving only one injection a day and so does away with the nuisance of multiple injections Experience has demonstrated however that it is not uniformly useful for all patients who require insulin in fact it is good for only about half such cases It has been found most beneficial in those patients who have a mild easily controlled form of the disease and in those who require only small or moderate doses of insulin and

case The quantity of any part of the diet may have to be varied from time to time the first changes being made usually in the carbohydrate content As the patient s tolerance for glucose improves, the carbohydrate content may be increased When glycosuria persists even in the face of a minimal carbohydrate content in the diet, a glucose free urine will often be brought about by increasing the fat content of the diet by 10 to 15 gm Therefore the physician must be prepared to make changes from time to time in the diet to suit the needs of the patient and to improve control of the diabetes A moderate amount of exercise such as short brisk daily walks adds further to the sugar metabolism in the body

Frequently the question of alcoholic beverages arises Generally they should be avoided In the mild diabetic however, it has been found that a single alcoholic drink followed immediately by the regular meal will not usually upset any balanced control that has been established

Insulin It has been estimated that approximately 50 per cent of diabetics can be treated successfully with diet alone particularly older persons with mild diabetes There are good authorities on the other hand who have recently stated that all patients with diabetes should have insulin treatment As a rule children will require the use of insulin

The various insulins in use today have given rise to a certain amount of confusion with some advocating one type and others advocating another type As with the antibiotics each type has its place when one knows how to use it

Regular and Crystalline Insulin These may be considered under one heading because their action is similar — that is short and intensive Crystalline insulin is zinc insulin that has been recrystallized and therefore contains only traces of inert foreign protein hence it causes fewer allergic reactions than regular or ordinary insulin

The glucose reducing effect of these insulins in diabetic patients is greatest about 4 hours after subcutaneous injection the effect waning in 8 to 12 hours Because of this several injections are required daily, which are determined by experience in relation to the food loads of the day Hence regular or crystalline insulin is to be given before each meal Also spoken of as short acting insulins they are perferred (1) in the new diabetic to bring him under adequate control rapidly ( ) in emergencies such as diabetic coma or unconsciousness from other causes infections or other situations in which the diabetes is out of control (3) in post operative care

increased by 5 to 10 units per day until the morning urine is sugar-free or until the fasting blood sugar approaches normal levels If glycosuria and hyperglycemia persist after meals supplementary regular insulin should be added until control is obtained, by use of the method already outlined for regular insulin — that is 8 units for 1 plus sugar 12 units for 2 plus sugar et cetera If finally a single daily injection of protamine insulin does not control the diabetes and multiple injections are required it is recommended that an insulin mixture be used as outlined in a subsequent paragraph

To reiterate protamine zinc insulin is most useful in obese mild or older diabetics with a relatively stable form of the disease for whom dosages under 40 units daily are sufficient and in whom fasting glucose levels are high in proportion to postcibal glycosuria

With any of the long acting insulins protamine zinc insulin globin insulin or insulin mixtures it is best to allow a 1 plus glycosuria for some time of each day as a safeguard to insulin reactions

Globin Insulin Globin insulin is a mixture of insulin in solution with a globin that is a fraction of beef hemoglobin It contains a small amount of zinc Devised as a long acting insulin globin insulin is somewhat intermediate in time of action between regular insulin and protamine zinc insulin At first it was used only in cases that reacted at night when on protamine zinc insulin or that manifested local reactions to the latter preparation More extensive experience has demonstrated that it is also an extremely useful preparation in certain thin young severe diabetics with a labile form of the disease who require more than 40 units per per day and in those with postcibal glycosuria heavy in relation to fasting glycemia When it is injected before breakfast its maximum effect occurs in the afternoon hours (12 noon to 6 p m) It has the distinct advantage of causing few local or other allergic reactions

Extremely severe labile or brittle' diabetics who are susceptible to sudden or violent shifts in glucose levels are controlled best by the use of globin insulin or by a protamine insulin mixture that contains excesses of regular insulin (see below)

Insulin Mixtures Such preparations consist of a mixture of unmodified (regular) insulin and protamine zinc insulin They may be prepared in two ways When the mixture is made in the syringe just prior to injection it is called an extemporaneous mixture when the combination is prepared in the vial it is called a premixed mixture The latter will keep for several months in a cold place

case The quantity of any part of the diet may have to be varied from time to time the first changes being made usually in the carbohydrate content As the patient s tolerance for glucose improves, the carbohydrate content may be increased When glycosuria persists even in the face of a minimal carbohydrate content in the diet, a glucose free urine will often be brought about by increasing the fat content of the diet by 10 to 15 gm Therefore the physician must be prepared to make changes from time to time in the diet to suit the needs of the patient and to improve control of the diabetes A moderate amount of exercise such as short brisk, daily walks adds further to the sugar metabolism in the body

Frequently the question of alcoholic beverages arises Generally they should be avoided In the mild diabetic, however, it has been found that a single alcoholic drink followed immediately by the regular meal will not usually upset any balanced control that has been established

Insulin It has been estimated that approximately 50 per cent of diabetics can be treated successfully with diet alone, particularly older persons with mild diabetes There are good authorities, on the other hand who have recently stated that all patients with diabetes should have insulin treatment As a rule children will require the use of insulin

The various insulins in use today have given rise to a certain amount of confusion with some advocating one type and others advocating another type As with the antibiotics each type has its place when one knows how to use it

Regular and Crystalline Insulin These may be considered under one heading because their action is similar — that is short and intensive Crystalline insulin is zinc insulin that has been recrystallized and therefor contains only traces of inert foreign protein hence it causes fewer allergic reactions than regular or ordinary insulin

The glucose reducing effect of these insulins in diabetic patients is greatest about 4 hours after subcutaneous injection, the effect waning in 8 to 12 hours Because of this, several injections are required daily, which are determined by experience in relation to the food loads of the day Hence regular or crystalline insulin is to be given before each meal Also spoken of as short-acting insulins they are perferred (1) in the new diabetic to bring him under adequate control rapidly (2) in emergencies such as diabetic coma or unconsciousness from other causes infections or other situations in which the diabetes is out of control (3) in post operative care

increased by 5 to 10 units per day until the morning urine is sugar-free or until the fasting blood sugar approaches normal levels If glycosuria and hyperglycemia persist after meals supplementary regular insulin should be added until control is obtained by use of the method already outlined for regular insulin — that is 8 units for 1 plus sugar 12 units for 2 plus sugar et cetera If finally a single daily injection of protamine insulin does not control the diabetes and multiple injections are required it is recommended that an insulin mixture be used as outlined in a subsequent paragraph

To reiterate protamine zinc insulin is most useful in obese mild or older diabetics with a relatively stable form of the disease for whom dosages under 40 units daily are sufficient and in whom fasting glucose levels are high in proportion to postcibal glycosuria

With any of the long acting insulins protamine zinc insulin globin insulin or insulin mixtures it is best to allow a 1 plus glycosuria for some time of each day as a safeguard to insulin reactions

Globin Insulin Globin insulin is a mixture of insulin in solution with a globin that is a fraction of beef hemoglobin It contains a small amount of zinc Devised as a long acting insulin globin insulin is somewhat intermediate in time of action between regular insulin and protamine zinc insulin At first it was used only in cases that reacted at night when on protamine zinc insulin or that manifested local reactions to the latter preparation More extensive experience has demonstrated that it is also an extremely useful preparation in certain thin young severe diabetics with a labile form of the disease who require more than 40 units per per day and in those with postcibal glycosuria heavy in relation to fasting glycemia When it is injected before breakfast its maximum effect occurs in the afternoon hours (12 noon to 6 p m) It has the distinct advantage of causing few local or other allergic reactions

Extremely severe labile or brittle diabetics who are susceptible to sudden or violent shifts in glucose levels are controlled best by the use of globin insulin or by a protamine insulin mixture that contains excesses of regular insulin (see below)

Insulin Mixtures Such preparations consist of a mixture of unmodified (regular) insulin and protamine zinc insulin They may be prepared in two ways When the mixture is made in the syringe just prior to injection it is called an extemporaneous mixture when the combination is prepared in the vial it is called a premixed mixture The latter will keep for several months in a cold place

who ordinarily do not fluctuate widely between hyperglycemia and hypoglycemia It is not usually very satisfactory for the severe cases or for very young or very thin diabetics

Several methods of application have been suggested, but in the easily controlled cases in which the use of this insulin is indicated, the simplest method and one of the most effective, is to control the glycosuria first with regular insulin and then transfer to protamine zinc insulin In the new case or in the uncontrolled old case the diabetes should be brought under control first with multiple daily injections of regular (ordinary) insulin as outlined previously then transfer to protamine zinc insulin giving a dose two thirds the one of regular insulin that has been found to control the patient s glycosuria For example, if a given patient requires for good control a total of 30 units of regular insulin in the 24 hour period in making the transfer one begins with a daily morning injection of 20 units of protamine zinc insulin Having made the change one must remember that it requires from 3 to 5 days for the individual to become stabilized on a given dosage Hence in regulating a patient s diabetes with protamine zinc insulin the trial dosage should be continued for 3 to 5 days before changing the dose again It has been found by experience that if the patient requires more than 30 or at most 40 units of protamine zinc insulin per day a mixture of protamine zinc and regular insulins should be used instead of protamine zinc insulin alone The reason for this is that the daytime food load produces hypergly cemia and glycosuria when more than 40 units per day are required Moreover in the hours when no food is taken hypoglycemia may result and this is the reason the reactions to protamine zinc insulin tend to occur in the early morning (12 midnight to 6 a m)

Occasionally in moderately severe diabetes even the long acting in sulins do not act long enough In them, when large doses of modified insulin are being required for control better results, sometimes with lower dosage, may be attained by dividing the total daily dose of long acting insulin into 2 parts giving 80 per cent of the dose in the morning and 20 per cent in the evening

It is unwise to depend upon protamine zinc insulin in any emergency need for insulin such as in diabetic coma in post-operative care and so on because as has just been emphasized, it is impossible to judge the effect of any given daily dosage until after several days of injections

Another method of treatment beginning directly with protamine zinc insulin is to give 10 units as the initial dose on the first day This is

NPH is a neutral protamine insulin modified by crystallization and contains 0 50 mg of crystallized protamine for every 100 units of insulin The action of NPH is similar in many respects to that of globin insulin and to that of a 2 1 mixture of regular and protamine zinc insulin It is most useful in the more labile severe diabetic not so successful in children One advantage it has over a 2 1 mixture is that it gives an intensified earlier action without reducing the duration of activity below 24 hours Like protamine zinc insulin it has a hypoglycemic effect that is nocturnal A transfer from other long acting insulins to NPH may be made directly, in the same dosage as the insulin that was being given

Another product NP 50 is too unstable by present methods of manufacture to be placed upon the market Other insulins that are being produced are approximately 2 1 mixtures It is being found that 2 1 mixtures in indicated cases are effective for about 80 per cent of the cases about 80 per cent of the time

Insulin Reaction In the initial regulation of the diabetic sometimes too much insulin may be used which fortunately will give the patient the experience of recognizing the symptoms of hypoglycemia With regular insulin these are often startling whereas with long acting insulins the symptoms may be so gradual as not to be recognized Every diabetic should be warned of the symptoms of hypoglycemia as well as those of hyperglycemia and still better should be made to carry an identification card labeling him as a diabetic with instructions to give sugar if he is found unconscious and to remove him to a hospital if no improvement appears in 15 minutes after sugar has been administered

For insulin tumefactions and atrophy of subcutaneous tissues there is no specific therapy The sites of injections should be varied The management of allergic reactions has been discussed under Regular Insulin Some recent evidence indicates that recrystallizing insulin preparations several times removes the impurities that cause certain allergic reactions

Insulin Resistance The exact cause and mechanism of insulin resistance is not known although it has been common knowledge for many years that in coma, infections allergic states endocrine disturbances (hyperthyroidism) hemochromatosis and certain forms of liver disease the insulin required to control glycosuria may be very high The term here is limited to those cases requiring more than 200 units per day In treatment change of the site of insulin injection may help if the resistance is only apparent and not real i e from improper ab

Insulin mixtures provide three advantages in treatment First, the regular insulin contained in them gives an intensified action at an earlier hour than protamine alone with the advantage of insulin action during the day along with the food load of mealtimes Second, the protamine action in the early morning hours is less intense, for, in effect, the mixture intensifies protamine action and at the same time lessens its prolonged effect Thirdly the proper mixture maintains a satisfactory duration so that only one injection per day is necessary

Insulin mixtures are not to be considered simply as intermediate in their action between regular and protamine zinc insulins They should be thought of as providing an insulin effect of variable degree of duration depending upon their over all rates of solubility and the release of active principle from the depot in the tissues They must be considered as new compounds not typical of the standard long-acting insulins

Insulin mixtures are to be given preferably in the morning Various combinations have had therapeutic trial — 1 1, 2 1 3 1, 3 2, of which the best at present is considered to be 2 1, i e two parts of regular insulin to 1 part of protamine zinc insulin Mixtures are to be made always from the same concentration that is, from U 40 or U 80 To transfer to an insulin mixture protamine zinc insulin alone is given daily and is increased gradually until satisfactory blood levels of glucose are maintained before breakfast Supplementary doses of regular insulin are then given during the day according to the precibal urine tests When conditions have become reasonably constant the total dosage is combined into a 2 1 mixture in the syringe and is given as a single dose before breakfast If daytime glycosuria and hyperglycemia persist the regular insulin content is increased slightly If post-absorptive (fasting) glycosuria and hyperglycemia persist the amount of protamine zinc insulin is increased slightly and thus the mixture is regulated to suit the needs of the individual patient In some respects the 2 1 and 3 1 mixtures are comparable in their action to globin insulin Yet because the regular insulin content in the mixture can be altered easier and better control can often be achieved with the mixture than with globin insulin

Insulin mixtures are indicated for use in the unstable brittle" diabetics who are otherwise difficult to control The extemporaneous mixtures may be difficult to apply in handicapped persons in those with poor vision, and in the illiterate For that reason there is present interest in newer forms of insulin of which NPH 50 is one

fections tend to lead to acidosis, dehydration coma, and death It is for this reason that discipline as emphasized at the beginning of this chapter is so necessary in the proper treatment and control of every diabetic patient Treatment of an impending acidosis should begin promptly with the first sign of excessive glycosuria. As a matter of rule, the routine testing for ketonuria should always be carried out in the presence of heavy glycosuria. Proper regulations of the diet and the insulin, rest, and adequate fluids including parenteral saline if the condition has progressed to the point of ketone excretion and lowered carbon dioxide combining power of the blood should be applied When any ketonuria is present it is best to admit the patient to a hospital at once, where careful regulation of his treatment can be carried out day and night Upon admission a quantitative blood and qualitative urine analysis for glucose should be made Whatever insulin product the patient has been on if any should now be changed to regular or crystalline insulin with injections at 6 hour intervals If the acidosis is the result of some complication particularly infection and a proper diet has been maintained, the same diet may be continued and the acidosis corrected simply by the use of larger i e adequate doses of regular insulin If, on the other hand dietary indiscretion is the cause a proper diet as already outlined should be instituted and regular insulin given in graded doses to control the hyperglycemia and glycosuria An adequate fluid balance should be maintained at all times

Diabetic coma constitutes a true medical emergency Admitting the patient to a hospital is imperative where a skilled team of physician, nurse and laboratory technician may co operate in bringing the condition under control as quickly as possible

The new interest and knowledge concerning alterations of potassium metabolism in diabetic coma call for modification of some previous methods of emergency treatment of coma This includes the administration of little or no glucose in the immediate treatment unfortunately too much glucose solution is still being utilized by many

The treatment of diabetic coma advised at present consists of the administration of large doses of insulin and saline solution to bring the condition under control as rapidly as possible with careful observation for possible hypopotassemia (hypokalemia)

General measures in the care of the patient help greatly in bringing about recovery The patient should be put to bed at once well covered with blankets taken from a warmer and surrounded by hot water bottles

sorption. The insulin may have to be given intravenously. Any infection should be treated and eradicated. Any metabolic disorder should be corrected. Meanwhile, and in those instances in which no corrective measures can be carried out, large doses of insulin must be administered, as many as 600 to 800 units per day, to control as well as possible the blood sugar levels and urinary excretion of glucose. Actually the need for the use of such high doses is extremely rare.

Complications in Diabetes

Infection. Certain infections are more likely to develop in diabetics than in non diabetics, such as skin infections (furuncles and carbuncles), urinary-tract infections, and respiratory-tract infections. At the same time an acute infection of almost any sort occurs more easily and more severely in uncontrolled diabetes than in controlled diabetes or in non diabetics. By the same token an existing infection often makes diabetes more difficult to bring under control than it normally would be. When a patient under satisfactory control begins to spill glucose, it is a good rule to suspect the presence of an infection and to look for it. It is of paramount importance in the treatment of any bacterial infection in the presence of diabetes to bring the diabetes under control as promptly as possible. While this is being done, the accepted methods of treatment for the given infection should be instituted. Because of their known high incidence, bladder infections, in particular, should be looked for in all females with diabetes mellitus. Once a diabetic has established a urinary-tract infection, a tendency always exists for it to recur.

So important is prevention of infection in the extremities, particularly the feet, that in every diabetic a good routine of foot care should be outlined at the beginning of treatment so as to prevent foot infection and possible gangrene of foot or foot and leg. The feet should be bathed each evening in warm, not hot, water and then well dried; a thin coating of lanolin should be applied between and under the toes. Trichophytosis must always be eliminated, as the breaks in the skin which it causes serve as portals of entry for bacteria. It should be treated as described under Dermatomycosis.

Toenails should be cut properly, calluses strictly avoided or carefully removed, and the extremities kept warm and dry at all times.

Diabetic Acidosis and Coma. Lack of control of the diabetes and in

amount depending upon the apparent need as indicated by the carbon-dioxide combining power the glucose concentration in the blood and the presence or absence of glycosuria are to be given at 4 hour intervals until the patient has fully recovered from the ketosis and is able to resume his diet Protamine zinc insulin should not be administered more often than once a day in such cases

Fluid and Electrolyte Balance Next in importance to insulin are correction of dehydration and restoration of depleted electrolytes, particularly sodium and chloride by the early continuous and adequate administration preferably intravenously, of warm isotonic solution of sodium chloride Usually the administration of normal saline solution should be begun at once 1000 to 1500 cc given slowly and this should be repeated once or twice in the first 6 hours The average case will require 4 to 5 liters within the first 24 hours much more may be needed *the essential is to correct the dehydration* When fluid by mouth is tolerated this route is preferable

In some patients peripheral veins may be collapsed so that intravenous injections are very difficult or even impossible Then the solution may be given subcutaneously in the inner aspects of both thighs with absorption accelerated by the injection of 1 0 cc (250 viscosity units) of hydase or alidase (hyaluronidase) into the rubber tubing attached to the hypodermoclysis needle Glucose and/or saline may be given by rectum by the Murphy drip apparatus

Further if other routes cannot be employed the fluid may be introduced very satisfactorily into the bone marrow of the sternum by means of a needle equipped with a beveled obturator the rate of flow through such a needle into the manubrium sterni of adults by gravity at 1 meter height will vary between 5 and 20 cc per minute

Diet in liquid form usually can be given by mouth within 4 to 6 hours after treatment has been started 3 or 4 ounces (90 to 120 cc) of water broth gruel tea with sugar orange juice or ginger ale given at 6 hour intervals If nausea or vomiting delays this glucose solution can be given intravenously as a 5 per cent solution in 0 9 per cent saline When liquids are being tolerated well semi solids and solids should be added to the diet with a gradual shift back to the diet formulated to the needs of the individual and his diabetes

Potassium Balance Potassium is contained principally in the cells of the body and with the dehydration that develops so rapidly in diabetic coma it is removed from the cells and excreted in the urine During

outside of the blankets (care being taken that the patient is not burned) or covered by an electric blanket Urine and venous blood specimens are to be obtained as soon as possible and sent immediately to the laboratory for prompt determination of glucose content The determination of the carbon-dioxide combining power of the blood should be made The stomach is to be emptied by stomach tube and washed out gently with warm water If there is abdominal distention, an enema should be given and/or rectal tube passed

Insulin Either regular or crystalline insulin alone or in combination with protamine zinc insulin should be given Crystalline insulin is preferable and is to be given as follows The first dose of crystalline insulin should be given subcutaneously in a dose of from 20 to 100 units The dose for the average patient is about 50 units If the patient is unconscious or in shock, an accompanying dose of the same size should be given intravenously A second dose of like amount is to be given subcutaneously half an hour later As a rule, it will be necessary to give two other doses of 50 units of regular insulin at half hour intervals The average patient in coma requires about 200 units of insulin within the first 2 or 3 hours of treatment Initial blood and urine determinations of glucose content should act as a guide After 2 or 3 hours another sample of blood and urine should be taken and its glucose content quantitated These should serve to indicate whether or not treatment should be pushed more energetically If, despite the large initial dose of insulin the blood values have shown little or no tendency to return toward normal even larger doses of insulin may need to be given more frequently By this time the patient should be able to void at hourly intervals so that subsequent administration of insulin may be gauged by the test of his urine and by the results of the use of regular insulin As the patient comes under control, the physician should begin to develop a proper diet to be given subsequently and should get the insulin dosage on a regular schedule

If protamine zinc insulin is used for the adult patient in coma, begin by giving 80 to 100 units of protamine zinc insulin and 60 units of crystalline insulin subcutaneously at different sites, adding possibly 40 units of crystalline insulin intravenously Subsequent doses should be of crystalline insulin the number of units being regulated according to the gravity of the clinical condition and the response to treatment Usually 50 units are to be given 4 to 6 hours after the initial dose and again after 8 or 12 hours Thereafter small doses 8 to 12 units the

Vol. VIII 353

glucose free adequate fluid intake and output and electrolyte balance attained When the operative procedure is of emergency nature pre operative blood and urine determinations of glucose are essential as a guide in the hours to follow It is well to administer 5 per cent glucose covered adequately with insulin just before the operation It is a good rule to give at the same time the number of units of insulin the patient has previously been using per 24 hours but this dosage should be divided into smaller and more frequent doses irrespective of meals

The surgery must be meticulously carried out with strictest technique Whether well controlled or not diabetic wounds are more susceptible to infection than similar wounds in non diabetics

After the operation it is best to give insulin frequently i e in small doses every 3 or 4 hours rather than infrequently in larger doses If needed all fluid and nutrients can be given parenterally covered with insulin or the patient can start on liquid followed soon by semi solid food with final resumption of the patient s regular diet Under such circumstances regular or crystalline insulin should be used For minor procedures of course there may be little change needed in the patient s regime although it is a good rule to consider a post operative upset in the diabetic almost inevitable and accordingly to watch for it

The anesthetic agent must be chosen with great care general anesthetics of long duration particularly ether and chloroform with their action on the liver have a most harmful effect on diabetes Local or block or nitrous oxide anesthesia are recommended when feasible Sodium pentothal likewise is relatively safe For amputations of lower extremities spinal anesthesia is the anesthesia of choice An anesthesia as short as is reasonable should always be employed and the surgery done as expeditiously as possible

Pregnancy in Diabetes For the pregnant woman known to have diabetes mellitus or who develops proved diabetes during pregnancy the following treatment is to be used Glycosuria during pregnancy with a normal fasting blood glucose in a patient not previously treated for diabetes mellitus is probably a renal glycosuria and requires no treatment other than careful observation to see whether diabetes mellitus does develop

With pregnancy established in a diabetic one must decide whether or not it should be allowed to continue Some have considered diabetes in both parents or in the families of both parents or a background of hypertension or vascular or renal disease in the pregnant diabetic woman as

acidosis there is immediate increased loss of potassium in the urine. It has been found that brisk diuresis and glucose solution lower the blood potassium level below the normal of 4.0 to 5.0 millequivalents per liter. For that reason parenteral glucose and diuresis are to be avoided in the initial treatment of diabetic coma. Fluids and electrolytes lost through dehydration should be replaced, as has already been discussed, but active diuresis should not be promoted.

The best single index of hypokalemia is a determination of the serum potassium level although it is not an infallible guide, since a considerable loss of potassium in the urine may occur before extracellular levels are seriously affected. Where laboratory facilities are not available or even when potassium determinations are possible careful attention should be paid to the clinical condition of the patient, the presence or absence of muscle weakness or paralysis, the urinary output, the changes in the electrocardiogram (rounded T waves of increased duration, low amplitude or inversion, prolongation of Q-T interval, and RST segments slightly depressed) and prominent U waves may be indicative of hypokalemia.

The manifestations of hypokalemia occur generally in the first 24 hours of treatment, but with the insulin and saline therapy just outlined the patient is usually conscious within 6 or 7 hours. At that point orange juice and oatmeal gruel, both high in potassium content, should be given by mouth to avert hypokalemia. Potassium chloride in doses of 2.0 to 4.0 gm by mouth constitutes good prophylaxis and good therapy. If potassium needs to be given parenterally, it may be administered intravenously as a 2.0 per cent solution of potassium chloride in 1000 cc of normal saline solution but *not with glucose*. More recently a combination of potassium and phosphate has been advocated for intravenous use. It should be cautioned that in any type of renal impairment or decreased urinary output from any cause, potassium should be administered very carefully or a fatal outcome may result from hyperkalemia. In the presence of hypokalemia glucose administration should be avoided.

Surgery in Diabetes. With proper control of the diabetes almost any type of surgery may be carried out as successfully as in the non-diabetic. Whether elective or emergency, the proper surgical care of the diabetic requires the closest co-operation between surgeon and internist.

When possible careful preparation should be given to the diabetic patient before surgery with normal glycemia and urine relatively

state should include sodium restriction, the use of 4.0 to 8.0 gm of ammonium chloride daily increased protein in the diet, and the administration of diuretics. Very useful in this connection is the daily subcutaneous administration of mercaptomerin sodium (Thiomerin Sodium) in 1.0 cc doses.

The greatest advance in the treatment of pregnancy in diabetics has come from the knowledge that most such women demonstrate frank hypo ovarianism associated with high blood levels of follicle stimulating hormone and that when this is corrected by proper replacement therapy, a much more normal course of pregnancy will occur resulting in a high percentage of healthy infants. Although this therapy is quite expensive it should be instituted early in pregnancy. Both stilbestrol and progesterone should be given intramuscularly in daily doses of 5 mg each up to the twentieth week of pregnancy. Thereafter, the dosage of each hormone should be increased by 5 mg every fourth week up to term by which time a total of 30 to 50 mg of each hormone is being given daily. In the case of infections with fever this dosage should be doubled. Some have used stilbestrol orally and the progesterone intramuscularly but such a method seems to be less efficient. Natural and synthetic estrogens seem to be equally effective.

Final consideration needs to be given to the *obstetrical management*. The size of the fetus as judged by x ray and palpation, and the tendency to premature death in utero influence the optimum time for and the best method of delivery. When the infant is large delivery should be preferably by caesarean section between the thirty sixth and thirty eighth week of gestation. Spinal anesthesia then is the anesthetic of choice. If normal labor occurs only small amounts of barbiturates and scopolamine should be given with the third stage of labor conducted under spinal or gas-oxygen anesthesia. Any disturbance in the diabetic balance should be treated as already outlined for emergency treatment of diabetes.

Management of Chronic Complications. Such complications as hypertension nephritis cardiac disease with or without decompensation all of which commonly occur in diabetics are to be treated in the same way as when they occur in non diabetics.

In diabetic coma with its dehydration and sodium and chloride loss a deviation of fluids may occur, giving rise to *extrarenal azotemia*. In its early stages this is a reversible condition therefore it must be recognized and treated promptly. In its more fulminating forms it leads to lower nephron nephrosis this may be reversible or it may lead to an early

strong indications for termination of the pregnancy Religious beliefs must be considered in this connection Spontaneous abortion may occur and solve the problem

If the pregnancy is to continue, certain chemical abnormalities peculiar to the pregnant diabetic woman are of paramount importance in her care during the gestation and the puerperium These center principally around (1) a lowered renal threshold for glucose, (2) an increasing need for protein and total calories in the diet, (3) an increasing requirement for insulin as the pregnancy progresses (4) water retention, and (5) imbalance of the sex hormones of pregnancy

The first of these low renal threshold for glucose requires frequent determination of blood glucose as a guide to insulin dosage with less reliance on urine glucose to prevent insulin reactions In the first trimester another cause of hypoglycemia is pernicious vomiting Here the insulin may need to be reduced but must not be discontinued it is better to risk hypoglycemia than acidosis The vomiting may be corrected by small dry concentrated feedings at frequent intervals or by administering parenterally the glucose equivalent of meals, the nutrients being covered with insulin Dimenhydrinate (Dramamine), 50 to 100 mg 3 times a day by mouth or by rectum is effective in some cases in stopping the pernicious vomiting of pregnancy As the pregnancy progresses into the second and third trimester it is usually necessary to increase the diet 25 to 50 per cent The protein should be increased to 1 5 to 2 0 gm per kilogram of body weight the carbohydrate and fat ratios being maintained as before The calories should be increased by 300 to 500 per day This increase of the food in the diet will involve using more insulin, but even without giving more food it is usually necessary to raise the insulin dosage during pregnancy Although a few women require no change the majority need as much as 50 per cent more insulin by the end of pregnancy than was used before Such higher dosages frequently must be reduced quickly after delivery to avoid insulin shock During and after pregnancy the best rule is to keep the urine as nearly free of excess glucose as possible without causing insulin reactions insulin dosages being determined by the amount of glucose in the blood and urine

Water retention as manifested by edema gain in weight hydremia hydramnios and fetal edema is a prominent and characteristic feature of pregnancy in the diabetic Such disturbances of water balance should be discounted in calculating calorie requirements The treatment for this

acetophenetidin and caffeine (Empirin Compound codeine meperidine (Demerol) and possibly morphine may be required for pain For prophylaxis daily vitamin B complex in 5 to 10 times the normal daily requirement in addition to the usual diet is definitely of value Some are advocating the routine use of vitamin B complex in the treatment of diabetes mellitus It is also thought by some that if neuritis develops with the use of protamine zinc insulin a return to the use of regular insulin may help clear it up

Diabetic complications of the eye that are amenable to therapy include cataracts Treatment of them should be carried out entirely by a competent ophthalmologist For diabetic retinopathy there is no specific treatment other than the measures carried out for generalized vascular disease Where there is hypertension with retinal hemorrhage in diabetes, vitamin P (Rutin) 20 mg 3 or 4 times a day given over a prolonged period of time may possibly be helpful but in our hands it has not been of much value

More and more conservative measures are becoming successful in the treatment of *diabetic gangrene* when it is seen early enough As emphasized earlier the best therapy is prevention by meticulous care of the feet If necrosis of tissue develops bed rest is imperative Great care should be exercised in not applying any excess heat to tissues that have an inadequate blood supply in an effort to stimulate local metabolism The part should be kept dry to avoid maceration of tissue Cleanliness must be carried out the part being soaked once or twice daily in lukewarm boric solution if any infection is present and dried thoroughly thereafter Systemic treatment for the infection should be given with the appropriate antibiotic agent

When the condition has been seen early i e in the pre gangrene stage Buerger exercises practiced 3 or 4 times a day are very useful In this stage mild vasodilators accompanied by anticoagulant therapy such as bishydroxycoumarin (Dicumarol) given as in the treatment of acute coronary thrombosis may be effectual

With progression of the lesion and increasing pain amputation will be necessary In this connection it must be remembered that the amputation will usually be required at a level considerably higher than is apparent from the appearance of the lesion The closest co operation between surgeon and internist becomes necessary The pre and post operative care should be instituted as outlined in the paragraph on surgery in diabetes

death In the treatmnt of extrarenal azotemia adequate fluid and electrolyte balance will correct the condition, provided kidney function is not significantly impaired In the treatment of lower nephron nephroses therapy is more difficult and less successful Conservative management for lower nephron nephrosis has proved the most helpful Four principles may be used as a guide (1) If shock is present it should be combatted vigorously with blood transfusions either whole blood or serum as required (2) In the stage of oliguria or anuria *fluids should not be forced*, as would be the natural tendency in trying to produce diuresis Rather fluid balance should be maintained as estimated from urine output, vomitus and insensible water loss This loss will average perhaps 2000 cc per 24 hours (3) Sodium and chloride balance should be maintained as calculated from daily determination of blood sodium and/or chloride levels Only enough saline should be given intravenously or subcutaneously each 24 hours to maintain blood sodium and chloride at normal levels A few advocate the use of slightly excessive amounts of sodium daily to produce a mild edema to help in the reduction of blood nitrogen values The remainder of the 24 hour fluid intake should be made up by giving 2½ or 5 per cent glucose in distilled water In the full blown clinical picture of lower nephron nephrosis with anuria the urinary secretion may be absent for from 10 to 14 days and then return There is in this situation no specific treatment to be carried out Above all *diuretics must be avoided* A soft nutritious diet should be instituted When urine function begins to return fluid and saline should be increased according to increased fluid loss and chloride depletion Daily blood chloride determinations should be continued as a guide Sometimes profuse diuresis will follow requiring large amounts of fluid 5000 to 6000 cc or more daily to maintain fluid and electrolyte balance Complete recovery usually takes several months

If renal function does not return and the patient is deteriorating a run on the artificial kidney is warranted

Concerning *intracapillary glomerulosclerosis*, described by Kimmelstiel and Wilson and so peculiar to the diabetic state there is no known specific treatment It should be treated as other forms of glomerulonephritis

Diabetic neuropathy is to be treated by rest to the affected part rigid control of the diabetes and the use of large doses of thiamin chloride 10 mg 5 times a day by mouth and vitamin B_{12} (Rubramin) 1000 micrograms parenterally, a day Acetylsalicylic acid or a mixture of this with

gives up 58 per cent of itself as carbohydrate thus avoiding insulin stimulation In principle then this diet (Conn diet) is one low in carbohydrate and high in protein with 3 meals a day The protein may be as much as 2 0 gm per kilogram of body weight daily Such a diet consists of 120 to 150 gm protein 50 to 75 gm carbohydrate and 150 to 175 gm fat — making up 2000 to 2250 calories The following is an example of such a diet (hypoglycemia diet)

Hypoglycemia Diet

Approximate values Protein 150 gm, fat 150 gm carbohydrate 75 gm calories 2 250

Breakfast

Choice of ½ grapefruit 4 oz. orange juice 6 oz tomato juice ½ cup orange or grapefruit sections
One egg
Broiled ham bacon or liver — average serving
1½ pieces zwiebach or ½ slice toast
Butter — generous serving
Coffee or tea with rich cream

Mid Morning

1 glass milk shake

Lunch

Choice of broiled lamb chop, creamed or broiled sweetbread creamed white fish salmon etc egg or cheese omelet broiled liver molded meat or chicken salad sliced cold red meat or chicken etc
Vegetable — see list allowed — ⅓ cup serving
Salad with mayonnaise or dressing
Low carbonhydrate dessert
Coffee or tea with cream

Mid Afternoon

Gelatinized milk rye crisp and butter

Chronic Hyperinsulinism Hypoglycemia

In this disorder the symptoms are the result of a rapid and severe fall in the level of circulating blood glucose due to overproduction of insulin by the pancreas The causes are several, but generally they can be grouped under (1) functional and (2) organic Treatment will be considered under these headings

Functional Hypoglycemia Into this category fall the instances of spontaneous hypoglycemia for which no organic cause, such as islet cell tumor carcinoma of the pancreas, or hepatic disease, is apparent The treatment resolves itself into control of the blood glucose level by diet to avoid excess stimulation of the production of insulin by carbohydrate In very mild cases the ingestion of small amounts of readily assimilable glucose such as orange juice a candy bar, or a lump of sugar is sufficient but in the more severe and chronic cases such use of glucose becomes too insulinogenic and will produce subsequent attacks In the chronic cases the carbohydrate moiety so large in the average American diet, must be reduced to a minimum or near minimum along with frequent feedings The planning of frequent feedings 6 or 8 through the day with low carbohydrate content may be sufficient This may be achieved readily by the free use of 3, 5, and 10 per cent vegetables in the diet reducing or eliminating the foods of higher carbohydrate

A low carbohydrate high-fat diet which will be slowly absorbed has been found to be effective This should include large amounts of 3 5 and 10 per cent vegetables which are absorbed more slowly th n higher carbohydrate foods and hence release dextrose into the blood stream in small quantities at a time Added to this should be a high fat content largely cream and butter which will delay the emptying time of the stomach and further retard dextrose absorption

Many patients with functional hypoglycemia are overweight from eating too much in their attempts to allay symptoms Strict individualization in diet outline is necessary and for them a reduction diet should be instituted as well For the average individual a diet of about 2000 to 2250 calories should be prescribed consisting of 70 to 90 gm of protein 100 to 150 gm of carbohydrate and 125 to 150 gm of fat This should be divided into 6 or 8 feedings through the day, including a late evening snack

Another diet may be outlined on the principle that protein slowly

is indicated by a blood glucose level below 40 mg per 100 cc during an attack *or a fasting* blood glucose level below 50 mg per 100 cc for the patient who has previously been on a normal diet Carcinoma of islet cells can give the same findings but this condition is the cause of hypoglycemic attacks much less frequently than is an adenoma In either event such levels of blood glucose indicate an organic cause of the hypoglycemia and call for surgery The following are given as indications for exploration of the pancreas in patients with hypoglycemia (a) absence of extra pancreatic causes of hypoglycemia, (b) abnormally low level of blood sugar values during symptoms and rapid relief of symptoms by the administration of dextrose (c) repeated fasting blood sugar values below 50 mg per 100 cc, when the patient has been eating an adequate diet (d) depression of the fasting blood sugar below 40 mg per 100 cc by carbohydrate reduction

If upon exploration an adenoma or carcinoma cannot be found to be present some have advocated the removal of a portion of the normal pancreas The results of such a procedure have not been uniformly successful It has been thought that the success of such a procedure probably means the inclusion of an adenoma that had been overlooked in the resected tissue More than one adenoma may be present and all islet cell tumor tissue must be removed to obtain a cure Corticotropin or cortisone given in the same dose and manner as for functional hypo glycemia gives excellent results

Hepatogenic hypoglycemia, when due to acute or chronic destruction and degenerative lesions of the liver may be treated successfully with diet alone by using a regime high in both protein and carbohydrate with a bedtime meal included At the same time careful x ray studies of the gall bladder as well as of liver function should be carried out in such cases, for the removal of a diseased gall bladder that is causing an ascend ing hepatitis can offer distinct help in this group of cases The following are given as indications for cholecystectomy in cases of hepatogenic hypoglycemia (a) postabsorptive hypoglycemia markedly intensified by restriction of dietary carbohydrate (b) postprandial hyperglycemia with intermittent glycosuria (c) hyperglycemic plateau type of dextrose tolerance curve *with abnormally low fasting level (d) evidence of im-* paired liver function discovered by other tests (e) evidence of a diseased gall bladder discovered by cholecystography and (f) presump tive elimination of other causes of chronic degenerative and destructive lesions of the liver

Dinner

Meat chicken or fish — large serving (at least 3 ounces)
Vegetable — ⅓ cup selected from list allowed
Salad with dressing
½ slice bread or 2 rye crisps or 1 corn muffin
Butter — generous serving
Low carbohydrate dessert
Coffee or tea with cream

Evening

1 glass milk shake and 1 arrowroot biscuit

Use only the following fruits and vegetables

Asparagus 4 stalks or 5 tips
Beans green or wax ½ cup
Celery 4 stalks of average size
Cucumber slices ⅓ cup
Lettuce 10 leaves or ¼ head
Endive 10 stalks
Spinach ½ cup
Tomatoes ½ cup or one 2" in diam
Cabbage ½ cup raw or cooked
Broccoli ½ cup
Cauliflower ½ cup
Egg plant ½ cup
Squash ½ cup
Turnip ½ cup
Beets ⅓ cup
Brussels sprouts ½ cup
Carrots ⅓ cup
Onion ½ cup
Rutabaga ½ cup
Peas ⅓ cup

Drug Therapy As already mentioned, for an acute attack of hypoglycemic symptoms the patient should take some form of concentrated glucose such as orange juice, a cube of sugar, and so on If the patient is unconscious a few cc of concentrated glucose solution (50 per cent) given rapidly intravenously, will relieve symptoms, or epinephrine, 0 5 to 1 0 cc of 1 1000 solution given subcutaneously, will be effective in arousing a patient from hypoglycemic stupor Such doses may also be given twice daily to supplement the high protein, low-carbohydrate diet Longer-acting substances such as ephedrine have not proved to be consistently effective Corticotropin, 40 to 80 mg intramuscularly, or cortisone 100 to 300 mg, intramuscularly or by mouth daily, reduced as hypoglycemia becomes controlled, gives excellent results

Organic Hypoglycemia In this much smaller group belong the instances of islet cell tumor of the pancreas, carcinoma of the pancreas, and hepatic disease In the former two, pancreatic surgery is the only method of proved therapeutic value In the latter cholecystectomy may be effective

Removal of an adenoma (or adenomata) of islet cells of the pancreas produces cure in such cases The probable existence of such an adenoma

Hypoglycemia

1 CONN J W The Spontaneous Hypoglycemias *Jour Amer Med Assoc* 1940 cxv p 1669
2 CONN J W Diagnosis and Management of Spontaneous Hypoglycemia *Jour Amer Med Assoc* 1947 cxxxiv p 130
3 McQUARRIE, T BAUER E G ZIEGLER M and WRIGHT W Metabolic and Clinical Effects of Pituitary Adrenocorticotrophic Hormone in Spontaneous Hypoglycemias, *Proc of First ACTH Conference* Mote J R P Blakiston Phila. 1950 p 225

Renal Glycosuria

Sometimes spoken of as renal diabetes, this condition ordinarily requires no treatment For a long time it was thought that diabetes mellitus never occurred in an individual with renal glycosuria, yet in an occasional case this happens Periodic observation of the patient should be carried out even after a diagnosis of renal glycosuria has been established, particularly if there is a family history of diabetes mellitus The glycosuria of low renal threshold may be decreased by the use of a high-protein, low-carbohydrate diet, which supplies glucose to the blood stream gradually, and thus spill-over from high glucose levels of the usual diet may be avoided Moderate exercise immediately after eating may also decrease this form of glycosuria

BIBLIOGRAPHY

Diabetes Mellitus

1 BEASER S B Diabetes Mellitus' *N E J Med*, 1950 ccxliii, pp 81 133

2 BUTLER A M Diabetic Coma *N E J Med*, 1950, ccxliii p 648

3 CASO E and STARE F Simplified Method for Calculating Diabetic Diets *Jour Amer Med Assoc* 1947 cxxxiii p 169

4 HARWOOD R Diabetic Acidosis ' *N E J Med*, 1951, ccxlv p 1

5 IZZO J L and CRUMP S L Clinical Comparison of Modified Insulins *J Clin Invest* 1950 xxix p 1514

6 JOHNS H Control of Diabetes Glycosuria an Unreliable Index to Glycemia *Ohio State Med Jour*, 1950 xlvi p 1073

7 MANN G B GARDNER C and ROOT H F ' Clinical Manifestations of Intercapillary Glomerulosclerosis *Am J Med*, 1949 vii p 3

8 MULTIPLE AUTHORS Symposium on Diabetes *Am J Med* 1949 vii p 585

9 ROOT H F Diabetic Coma versus Diabetic Nephropathy " *N E J Med*, 1951 ccxlv p 765

10 SHUMAN C R and FRANCIS R B NPH Insulin in Diabetic Patients with Complications *Am Jour Med Sc*, 1951, ccxxii, p 179

11 TUYNMAN P E and WILHELM S K Potassium Deficiency Associated with Diabetic Acidosis *Ann Int Med*, 1948, xxix, p 356

aqueous pitressin and deposited by forceps into alternate nostrils at the level of the middle turbinates every 3 to 4 hours

Capsules of posterior pituitary powder, containing 45 mg each, may be obtained The contents of 1 capsule may be snuffed into the nose or applied by insufflation 3 or 4 times daily

Other Measures Some advise the restriction of salt to 3 or 4 gm per day but otherwise a regular diet should be given A drastic reduction of fluid intake is not necessary but a gradual curtailment of fluid as urine output decreases under pitressin therapy is advisable to avoid water intoxication that may result from increased water intake with decreased water elimination

Drainage of spinal fluid may be tried but is usually not effectual in decreasing diuresis Amidopyrine (Pyramidon) has had some trial but its use is not advised because of its lack of striking efficacy and the dangers of agranulocytosis from its use Thyroid ablation is also not advocated

Gout

The treatment of gout consists of management of (1) acute gout (2) inter critical or asymptomatic gout and (3) chronic gout

Acute Gout Since acute gout usually manifests itself with very acute and painful arthritic symptoms bed rest with immobilization of the affected part should be instituted promptly All trauma to the affected joint and all avoidable movements must be prevented As the toes or feet are involved so commonly a cradle over the legs to avoid even the weight of bed clothing is desirable Massage is not indicated, but hot or cold compresses may be tried although usually they are not very helpful

Colchicine in tablet form is the remedy of choice being more effective than the wine or tincture of colchicum Colchicine should be started promptly 0 50 mg being given by mouth every hour day or night until the attack has been abated or nausea and diarrhea occur This usually requires 10 to 15 tablets and with recurrent attacks the patient soon learns how many will be needed to control the symptoms and yet not give gastro intestinal disturbances If such a course of colchicine fails to give desired relief a second course should be given after a lapse of 2 or 3 days

With onset of gastrointestinal symptoms colchicine should be stopped and if these symptoms do not subside promptly, camphorated tincture

Renal Glycosuria

Sometimes spoken of as renal diabetes, this condition ordinarily requires no treatment For a long time it was thought that diabetes mellitus never occurred in an individual with renal glycosuria, yet in an occasional case this happens Periodic observation of the patient should be carried out even after a diagnosis of renal glycosuria has been established, particularly if there is a family history of diabetes mellitus The glycosuria of low renal threshold may be decreased by the use of a high-protein, low-carbohydrate diet, which supplies glucose to the blood stream gradually, and thus spill over from high glucose levels of the usual diet may be avoided Moderate exercise immediately after eating may also decrease this form of glycosuria

BIBLIOGRAPHY

Diabetes Mellitus

1 BEASER S B Diabetes Mellitus' *N E J Med*, 1950, CCXLIII pp 81 133
2 BUTLER A M 'Diabetic Coma *N E J Med*, 1950 CCXLIII p 648
3 CASO E and STARE, F Simplified Method for Calculating Diabetic Diets *Jour Amer Med Assoc* 1947, CXXXIII p 169
4 HARWOOD R 'Diabetic Acidosis' *N E J Med*, 1951 CCXLV p 1
5 IZZO J L and CRUMP S L Clinical Comparison of Modified Insulins ' *J Clin Invest* 1950 XXIX p 1514
6 JOHNS H Control of Diabetes Glycosuria an Unreliable Index to Glycemia *Ohio State Med Jour*, 1950 XLVI, p 1073
7 MANN G B GARDNER C and ROOT H F Clinical Manifestations of Intercapillary Glomerulosclerosis *Am J Med*, 1949 VII p 3
8 MULTIPLE AUTHORS Symposium on Diabetes, *Am J Med*, 1949 VII p 585
9 ROOT H F Diabetic Coma versus Diabetic Nephropathy *N E J Med*, 1951 CCXLV p 765
10 SHUMAN C R and FRANCIS R B NPH Insulin in Diabetic Patients with Complications *Am Jour Med Sc*, 1951 CCXXII p 179
11 TUYNMAN P E and WILHELM S K Potassium Deficiency Associated with Diabetic Acidosis *Ann Int Med*, 1948 XXIX, p 356

as this has only slight addiction propensities If this does not control the pain use codeine phosphate 30 to 60 mg , or better, dihydromorphinone (Dilaudid) hydrochloride 2 mg , or even morphine sulfate 8 mg all to be given hypodermically and repeated as needed for recurring persisting pain It is to be remembered that these three are drugs causing addiction increasingly so in the order in which they have been listed and hence they should be used with great circumspection

The patient should be given a simple bland diet and an abundant in take of fluid to promote a urine excretion of 1500 to 2000 cc daily Along with this it is well to administer alkalies either as sodium bicarbonate 2 0 to 4 0 gm 3 to 4 times daily or potassium citrate 1 0 to 2 0 gm both by mouth to keep the urine alkaline The latter is preferred, if there exists any contraindication to sodium intake. Alkalinization of the urine is desirable particularly for those who have previously experienced renal colic or have had urate stones demonstrated since the precipitation of urate crystals in an acid urine is to be expected and may lead to formation of calculi or increase in size of any already present

Unlike most other forms of chronic arthritis in which prolonged con valescence is usually essential, the patient with acute gout should be en couraged to resume full physical activity as soon as the attack has sub sided

Colchicine may be used as a therapeutic test on a patient in whom a positive diagnosis of gout may be difficult to establish, since colchicine has only slight effect in relieving the joint symptoms of a suppurative arthritis an acute Heberden s node rheumatoid arthritis or rheumatic fever its effect is almost specific for gout For such trial colchicine is to be given as just outlined for Acute Gout

Asymptomatic and Intercritical Gout Asymptomatic gout is the term used for increased uric acid substances in the blood in the absence of genito urinary tract obstruction renal failure or leukemia in individuals who have or have had no symptoms of gout, especially painful joints but who *may* have tophi The term intercritical gout is used for the stage in which the patient who has had symptoms of gout is symptomless

Very generally no therapy is advised for asymptomatic gout beyond the measures of general hygiene avoidance of obesity and moderation in consumption of a balanced diet normal in its proportions of protein fat carbohydrate and vitamins A few recommend for these patients the same drug therapy as advised in intercritical gout

For intercritical gout most physicians advise colchicine, 0 5 mg by

CHAPTER XXXIII

DISTURBANCES OF WATER AND URIC ACID METABOLISM

Diabetes Insipidus

In the treatment of diabetes insipidus the presence of a causative pituitary neoplasm or syphilis should be sought and, if found, appropriate treatment should be instituted. If surgery is indicated, the patient should be given pituitrin before operation by one of the methods to be described, in order to prevent dehydration and distention of the urinary bladder. If diabetes insipidus is associated with xanthomatosis, x ray therapy should be given to the skull; this may be helpful to both conditions.

In the vast majority of the cases, however, the etiology is unknown, and the most that may be accomplished is a control of the symptoms, particularly polydipsia and polyuria. A spontaneous cure does occur occasionally.

The symptoms of diabetes insipidus will be relieved quite specifically by the application of posterior pituitary substance in one form or another. This is true regardless of the etiology. Excellent control can be secured by the subcutaneous or intramuscular injection of vasopressin tannate (pitressin tannate in oil). This gives a slow and prolonged action, 0.3 to 1.0 cc., giving relief of symptoms for 36 to 48 hours. Hence, one injection every other day is usually sufficient. The dosage and time interval should be regulated according to the needs of the individual patient. In some 0.3 cc. may be sufficient; in others 1.4 cc. may be effective for 4 or 5 days. The effectiveness does not wear off, and such a preparation may be used indefinitely. This procedure has the disadvantage of requiring repeated injections.

When the parenteral route is undesirable, the application by intranasal route of either pituitary solution or powder gives excellent results. Aqueous pitressin may be sprayed into the nostrils at intervals throughout the day, or a pledget of cotton may be soaked with 0.5 or 1.0 cc. of

individual with hyperuricemia Post operative gout can usually be prevented by the administration of 2 to 3 tablets of colchicine 0 5 mg daily for 3 days before and 3 days after operation The prophylactic use of salicylates and probenecid in the doses recommended for intercritical gout serve to lower uric acid levels in the serum and may also be helpful in preventing attacks

Precipitation of attacks of acute gout have occurred following the intramuscular injection of liver extract or of a mercurial diuretic Caution should be used with these drugs in any patient with a background of gout

Chronic Gout The management of the chronic joint manifestations should combine the procedures already outlined for acute gout and intercritical gout, especially those for the latter, along with the measures generally used in the treatment of chronic arthritis In gouty arthritis corpulence should be particularly avoided Diet should be as discussed for intercritical gout

The specific drugs for chronic gout are the same as for the acute attack but with continued and less frequent administration Many prefer to use colchicine and salicylates together, the former continuously in doses of 0 5 mg twice daily the latter, 0 6 gm 3 times daily only when joint distress exists Probenecid (Benemid) 0 5 to 1 0 gm a day is also useful in combination with colchicine and gives excellent results If the patient is a stone former, small doses of alkali, sodium bicarbonate 4 0 gm 3 or 4 times a day may be helpful

Usual exercises such as short brisk walks should be taken Long, fatiguing hikes and sports should be avoided Massage spa baths hydrotherapy and various local measures are useful when given in moderation

For deformed joints corrective surgery is advised and for painful ulcerated large deforming or mechanically disturbing tophi, surgical excision should be employed Even if secondarily infected the wounds of simple excision or debridement heal well in gout Before any such surgical procedures are carried out the patient should be given 2 or 3 daily doses of 0 5 mg of colchicine, the same doses should be given for 3 days following the operation and probenecid (Benemid) 1 0 gm daily or acetylsalicylic acid, 0 6 gm 3 times a day for a week prior to and for 2 weeks following surgery

Extensive vascular disease affecting the heart and kidneys with or without hypertension occurs commonly in older patients with gout of long duration They should receive the same treatment as would be

of opium [paregoric], 4.0 cc. should be given every 3 hours in case of nausea or after every second or third stool. In case of stomach irritation from paregoric another constipating agent such as aluminum hydroxide and kaolin (Kaomagma) may be given in tablespoon doses.

More recently probenecid (Benemid) in a dose of 0.5 to 2.0 gm. daily by mouth has been found very effective in the interval treatment of gout. The dose given depends on the response of the patient. When this drug or the salicylates are given, the urine should be kept alkaline with sodium bicarbonate or potassium citrate as recommended below. Colchicine should be given as usual during the acute attack.

Acetylsalicylic acid or sodium salicylate should be given, if probenecid is not used, in a dose of 0.6 to 1.0 gm. every 3 or 4 hours, to aid in relieving pain and to increase uric acid elimination. When colchicine causes too great gastro-intestinal disturbance, salicylates or probenecid should be used in its place.

Cinchophen and neocinchophen, because of their toxic action on the liver, have lost favor in the treatment of acute gout and are usually not advised. Nevertheless, some feel that their use is warranted when colchicine and/or salicylate fail. If used, cinchopen (Atophan) or neocinchophen should be given by mouth, 0.5 gm. every 4 hours.

More recently, cortisone and corticotropin have been found to have a marked ameliorating effect on the joint symptoms of gout with increased urinary uric acid excretion and a concomitant fall in serum uric acid levels. With the present knowledge of their side effects after prolonged administration, however, it would seem wisest, if they are to be used at all, to confine their application to patients with acute attacks of gout. Cortisone may be given orally or intramuscularly in a dose of 100 mg. twice a day for the first several days and thereafter 50 mg. twice a day for a few days more. Corticotropin is given in a similar manner, beginning with 40 mg. intramuscularly, followed by subsequent doses of 20 or 40 mg. as needed. One injection of 40 mg. of corticotropin may suffice to bring the acute pain under control, with the usual measures of colchicine and salicylates then instituted to relieve subsequent symptoms.

Certain patients who do not respond well to colchicine obtain excellent results by the use of these hormones in small doses along with the colchicine.

In some patients pain may be very severe and not controlled by the measures already advised. For such a patient, first meperidine (Demerol) hydrochloride should be tried in hypodermic doses of 0.1 to 0.15 gm.

CHAPTER XXXIV

DISTURBANCES OF FAT METABOLISM

Obesity

It has become well established that obesity is the result of the intake of calories in excess of the needs of the particular individual with more recently the recognition of the importance of a psychic component The part now attributed to the endocrines is that they may determine the pattern of the obesity if the individual becomes overweight

With this point of view the present approach to the treatment of obesity requires an attempt to analyze the abnormal appetite Two causes are common habit and neurosis Often the child copies the eating habits of the parents which, when continued after the growth years result in obesity in adult life The neurotic factor may occur singly or together with habit in which hyperorexia results from simple restlessness mental depression frustration or as a gratification for some unsatisfied desire The end result is the same the ingestion of calories in excess for that particular individual This leads to obesity in a high percentage of these people Unfortunately obesity is an exceedingly common disease and one that is a real menace to a large segment of our population Ideally the normal individual should weigh approximately the same at 50 years of age as he did at 25 years The ideal weight for a 5 foot female is 105 pounds For each inch above 5 feet, another 5 pounds should be added The ideal male of 5 feet should weigh 115 pounds and an additional 5 pounds should be added for each inch over 5 feet

Variations in body build play an important role and must be considered when more accurate evaluation of the weight is desired The following table prepared by the Metropolitan Life Insurance Company of New York is excellent for this purpose

mouth once a day, every other day or on some other schedule of intermittent dosage as found effective by the method of trial and error. Colchicine will prevent attacks of acute gout or greatly decrease their severity. An intelligent patient is soon able to guide himself in taking colchicine so as to obtain good results.

Other drugs that increase urinary excretion of urate bodies are salicylates, cinchopen, and probenecid. These are effective in intercritical gout. Cinchophen and neocinchophen, however, are being used less and less because of the potential danger of serious hepatitis developing after they have been given, since even one small dose has resulted in such hepatitis; it is wisest not to use them at all. For intercritical gout sodium salicylate or acetylsalicylic acid should be given in mouth dosage of 3.0 to 6.0 gm per day. Even better, probenecid (Benemid) may be used in a dose of 0.5 gm by mouth daily for 1 week and subsequently increased to 0.5 gm 2 to 4 times a day. Evidence now available indicates that therapy with this drug leads to disappearance of tophi in some cases. Care should be taken to keep the urine alkaline in order to prevent stone formation in the urinary tract.

There remains no real unanimity with regard to *diet* or *alcoholic beverages* in asymptomatic and intercritical gout. There is agreement that these patients should have a diet with average normal values for protein, fat, and carbohydrate with vitamins sufficient to meet present accepted standards or somewhat more than the amount regarded as the minimal daily needs of man. Calories per day should be low enough to prevent any excess in body weight or to reduce it to normal when it is above generally accepted values of normality. Most physicians advise against foods such as liver, kidneys, thymus, and pancreas (sweet breads), anchovies, sardines, caviar, shad roe, and other fish eggs, and pig or calf brains, which are high in purine content. There is increasing agreement that a moderate amount of alcoholic beverages of any type, not observed to have caused gouty attacks, is allowable for patients having or having had any form of actual gout, but that patients potentially gouty will be wise not to use them. All of these patients, unless they are edematous from some renal or cardiac complication, should maintain a fluid intake sufficient to insure a 24-hour urine output of 2000 cc.

Under *prevention* in intercritical gout should be mentioned trauma and surgery. Since long hikes, such as hunting in the woods in the fall of the year, may precipitate an attack of gout, such stresses should be avoided. Any surgical operation may also precipitate an attack in an

When the weight of the average patient is compared with these tables, it will be readily seen that being overweight is a common failing Un fortunately, it is commonly accepted as a sign of good health Actually, it can and often does do serious harm Statistical studies show that there is a rapid increase in mortality rate as the degree of overweight increases The following data illustrates this point

AGES 45 TO 50

Pounds Overweight	*Per Cent Increased Mortality*
10	8
20	18
30	28
40	42
50	56

Of first importance in beginning the treatment of obesity is a sincere determination on the part of the patient to lose weight Beneficial results are seldom obtained when the physician has to coax The dietary treatment consists of a strict regulation of sub calorie intake with a view to breaking old habits such as *munching and having midnight snacks* and the development of new ones Whether one prescribes a 500 calorie or a 1 00 calorie diet depends upon the food habits of the individual how much weight is to be lost, and the rapidity with which it is to be lost Usually it is safest from the standpoint of continued good health as well as cosmetic results to lose no more than 1 to 1½ pounds per week over any extended period of time In the first week or two on a new and enthusiastic regime 4 or 5 pounds may be lost This is a normal happen ing It is well to point out that because of water retention by the break ing down of fat tissue in the third to fifth weeks no weight may be lost in fact there may be a slight gain in weight Water retention may also retard weight loss It is this fact that may dampen the patient s enthusiasm at the end of a month and may often cause failure in the entire program unless the individual is warned beforehand Following such an apparent standstill without change in the diet weight loss will occur again and continue ordinarily at a rate of 1 to 2 pounds per week down to the desired level of weight to be attained

Diet Metabolic studies have shown that a diet containing as few

given non-gouty individuals with these conditions There is no specific treatment available for the chronic renal disease so often complicating chronic gout It should be managed as described for chronic Bright's disease Pyelonephrosis and cystitis, if they occur, should be treated promptly with antibiotics or other antibacterial drugs selected on the basis of the infecting organism or organisms If there is obstruction to urine outflow anywhere this should be corrected by appropriate surgical procedures

BIBLIOGRAPHY

Diabetes Insipidus

1 BLOTNER H "Diabetes Insipidus" *Oxford Syst Med*, 1950 IV, p 179

Gout

1 GUTMAN A B and YU T F "Effects of Adrenocorticotropic Hormone (ACTH) in Gout, *Am J Med*, 1950 IX p 24
2 SCHNITKER M A and RICHTER, A B Nephritis in Gout *Am. Jour Med Sc*, 1936 CXCII p 241
3 TALBOTT, J H Medical Progress Gout and Gouty Arthritis" *N Y Med* (No 8) 1948 IV p 17
4 THORN G FORSHAM P FRAWLEY T HILL S, ROCHE, M STAEKELIN D and WILSON D Clinical Usefulness of ACTH and Cortisone *N E J Med* 1950 CCXLII pp 783 8 4 865
5 GUTMAN A B "Some Recent Advances in the Study of Uric Acid Metabolism and Gout' *Bull New York Acad Med*, 1951 27, p 144
6 PASCALE L R DUBLIN A and HOFFMAN W S Therapeutic Value of Probenecid (Benemid) in Gout" *Jour Amer Med Assoc*, 1952 149, p 1168

When the weight of the average patient is compared with these tables, it will be readily seen that being overweight is a common failing Unfortunately it is commonly accepted as a sign of good health Actually it can and often does do serious harm Statistical studies show that there is a rapid increase in mortality rate as the degree of overweight increases The following data illustrates this point.

AGES 45 TO 50

Pounds Overweight	*Per Cent Increased Mortality*
10	8
20	18
30	28
40	42
50	56

Of first importance in beginning the treatment of obesity is a sincere determination on the part of the patient to lose weight Beneficial results are seldom obtained when the physician has to coax The dietary treatment consists of a strict regulation of sub calorie intake with a view to breaking old habits such as *munching and having midnight snacks and* the development of new ones Whether one prescribes a 500 calorie or a 1200 calorie diet depends upon the food habits of the individual how much weight is to be lost and the rapidity with which it is to be lost Usually it is safest from the standpoint of continued good health as well as cosmetic results to lose no more than 1 to 1½ pounds per week over any extended period of time In the first week or two on a new and enthusiastic regime 4 or 5 pounds may be lost This is a normal happening It is well to point out that because of water retention by the breaking down of fat tissue in the third to fifth weeks no weight may be lost in fact there may be a slight gain in weight Water retention may also retard weight loss It is this fact that may dampen the patient s enthusiasm at the end of a month and may often cause failure in the entire program unless the individual is warned beforehand Following such an apparent standstill without change in the diet weight loss will occur again and continue ordinarily at a rate of 1 to 2 pounds per week down to the desired level of weight to be attained

Diet Metabolic studies have shown that a diet containing as few

TABLE XII

Desirable Weights for Men—Ages 25 and Over				
Height (with shoes)		Weight in Pounds (as ordinarily dressed)		
		Small Frame	Medium Frame	Large Frame
Feet	Inches			
5	2	116 125	124 133	131 142
5	3	119 128	127 136	133 144
5	4	122 132	139-140	137 149
5	5	126 136	134 144	141 153
5	6	129 139	137 147	145 157
5	7	133 143	141 151	149 162
5	8	136-147	145 156	153 166
5	9	140 151	149 160	157 1,0
5	10	144 155	153 164	161 175
5	11	148 159	157 168	165 180
6	0	152 164	161 173	169 185
6	1	157 169	166 178	174 190
6	2	163 175	171 184	179-196
6	3	168 180	176 189	184 02

Desirable Weights for Women Ages 25 and Over				
Height (with shoes)		Weight in Pounds (as ordinarily dressed)		
		Small Frame	Medium Frame	Large Frame
Feet	Inches			
4	11	104 111	110-118	11, 127
5	0	105 113	112 120	119-129
5	1	107 115	114 122	121 131
5	2	110-118	117 125	124 135
5	3	113 121	120-128	127 138
5	4	116 125	124 132	131 142
5	5	119 128	127 135	133 145
5	6	1 3 132	130-140	138 150
5	7	126 136	134 144	142 154
5	8	129 139	137 147	145 158
5	9	133 143	141 151	149-162
5	10	136-147	145 155	152 166
5	11	1,9-150	148 158	155 169
6	0	141 153	151 163	160-174

The normal values for children, according to Barach, are as follows

TABLE XII

Normal Height — Weight ½ to 21 Years

Age Years	Boys Height Inches	Boys Weight Pounds	Girls Height Inches	Girls Weight Pounds
½	26	17	26	16
1	29	21	29	20
2	33	26	33	25
3	36	31	36	30
4	39	35	39	34
5	42	38	41	37
6	45	43	44	43
7	47	50	47	47
8	49	55	49	54
9	51	61	51	60
10	53	67	53	67
11	55	75	55	74
12	57	81	57	82
13	59	90	60	94
14	6	103	62	105
15	64	112	63	112
16	66	126	64	117
17	67	133	64	122
18	68	138	65	124
19	69	138	65	126
20	69	139	65	1 6

Suggested Day's Menu

Breakfast	*Lunch*	*Supper*
Bread — ½ slice	Lean meat — 3 oz.	Lean meat — 3 oz.
No butter	Cucumber salad — ½ cup	Cole slaw — ½ cup (mineral oil dressing)
Skimmed milk — ¾ cup	Asparagus — ½ cup	Broiled tomato — ½ cup
Poached egg — 1	Water packed strawberries — ¼ cup	Watermelon balls — ¾ cup
Coffee	Skimmed milk — ¾ cup	Skimmed milk — ¾ cup
	Tea	Tea

Under ordinary circumstances, where some but not a great deal of weight needs to be lost, many prefer to prescribe a diet of 1000 to 1200 calories As a matter of discipline it is sometimes necessary to outline a rigid regime of foods to be eaten and foods to be strictly avoided as shown in the appended sample

1 00 Calorie Diet

Carbohydrate 140 gm. protein 80 gm. fat 35 gm (See Table IX page 405 and Table XI pages 407 408)

Breakfast One 10 per cent fruit — ½ cup or juice of 10 per cent fruit — ½ cup
Bread — 1 slice whole wheat or white, toasted if desired
Butter — 1 teaspoonful
Skimmed milk — ¾ cup
Egg — 1, cooked any way but fried
Tea or coffee no cream or sugar

Dinner Lean meat or fish or cheese or chicken — large serving (3 oz.) or cottage cheese — ½ cup
Note 1 egg may be substituted for each ounce of meat or any combination of fruits and vegetables equal to 30 per cent.
One 15 per cent vegetable — ½ cup
One 10 per cent fruit — ½ cup
Bread 1 slice
Butter 1 teaspoonful
Skimmed milk or plain buttermilk ¾ cup
Tea or coffee no cream or sugar

as 500 calories, properly balanced, can be used safely in a weight reduction regime This is an essentially high-protein diet Unless excessive exercise is used with it, it does not lead to any significant acidosis Such a diet should be low in fat and adequate in vitamins Fortunately leafy vegetables, which make up a large part of such a diet, are adequate in vitamins and are bulky enough to give satiety Following is a sample of a 500 calorie diet

500 CALORIE DIET

Carbohydrate 36 gm protein 65 gm, fat 13 gm (See Table IX page 405 and Table XI pages 407 408)

Breakfast Bread — ½ slice whole wheat or white toasted if desired
No butter
Skimmed milk — ½ cup (4 oz)
Egg — 1 cooked any way desired except fried (if scrambled do not add any extra fat)
Tea or coffee no cream or sugar

Dinner Very lean meat or fish or chicken — large serving (3 oz) or cottage cheese — ½ cup
Raw or leafy vegetables from list 1 as desired
One 5 per cent vegetable — ½ cup
One 10 per cent vegetable — ¼ cup
Tea or coffee no cream or sugar

Supper As for dinner

Note You are to eat only the foods listed on this diet and no candy soft drinks pastry cake, cookies ice cream, pudding gravy dressing, sauce nuts popcorn potato chips etc
Clear soups (fat free), bouillon cubes, mayonnaise made with mineral oil clear tea and coffee vinegar saccharine or cyclamate (Sucaryl) may be used in the diet without counting Supplemental vitamin therapy is usually wise when a borderline diet of this type is long continued Usually one capsule or tablet containing the normal daily vitamin requirements should be given

SUGGESTED DAY'S MENU

Breakfast	*Lunch*	*Supper*
Bread — ½ slice	Lean meat — 3 oz	Lean meat — 3 oz
No butter	Cucumber salad — ½ cup	Cole slaw — ½ cup (mineral oil dressing)
Skimmed milk — ¾ cup	Asparagus — ½ cup	Broiled tomato — ½ cup
Poached egg — 1	Water packed strawberries — ¼ cup	Watermelon balls — ¼ cup
Coffee	Skimmed milk — ¾ cup	Skimmed milk — ¾ cup
	Tea	Tea

Under ordinary circumstances where some but not a great deal of weight needs to be lost, many prefer to prescribe a diet of 1000 to 1200 calories As a matter of discipline it is sometimes necessary to outline a rigid regime of foods to be eaten and foods to be strictly avoided as shown in the appended sample

1200 CALORIE DIET

Carbohydrate 140 gm protein 80 gm fat 35 gm (See Table IX page 405 and Table XI pages 407 408)

Breakfast One 10 per cent fruit — ½ cup or juice of 10 per cent fruit — ½ cup
Bread — 1 slice whole wheat or white toasted if desired
Butter — 1 teaspoonful
Skimmed milk — ¾ cup
Egg — 1, cooked any way but fried
Tea or coffee no cream or sugar

Dinner Lean meat or fish or cheese or chicken — large serving (3 oz.) or cottage cheese — ½ cup
Note 1 egg may be substituted for each ounce of meat or any combination of fruits and vegetables equal to 30 per cent.
One 15 per cent vegetable — ½ cup
One 10 per cent fruit — ½ cup
Bread 1 slice
Butter 1 teaspoonful
Skimmed milk or plain buttermilk ¾ cup
Tea or coffee no cream or sugar

as 500 calories, properly balanced, can be used safely in a weight reduction regime This is an essentially high protein diet Unless excessive exercise is used with it, it does not lead to any significant acidosis Such a diet should be low in fat and adequate in vitamins Fortunately leafy vegetables, which make up a large part of such a diet, are adequate in vitamins and are bulky enough to give satiety Following is a sample of a 500-calorie diet

500 Calorie Diet

Carbohydrate 36 gm protein 65 gm fat 13 gm (See Table ix page 405 and Table xi pages 407 408)

Breakfast Bread — ½ slice whole wheat or white toasted if desired
No butter
Skimmed milk — ½ cup (4 oz)
Egg — 1 cooked any way desired except fried (if scrambled do not add any extra fat)
Tea or coffee no cream or sugar

Dinner Very lean meat or fish or chicken — large serving (3 oz) or cottage cheese — ½ cup
Raw or leafy vegetables from list 1 as desired
One 5 per cent vegetable — ½ cup
One 10 per cent vegetable — ¼ cup
Tea or coffee no cream or sugar

Supper As for dinner

Note You are to eat only the foods listed on this diet and no candy soft drinks pastry cake, cookies ice cream, pudding gravy dressing sauce nuts popcorn potato chips etc
Clear soups (fat free) bouillon cubes, mayonnaise made with mineral oil clear tea and coffee vinegar, saccharine or cyclamate (Sucaryl) may be used in the diet without counting Supplemental vitamin therapy is usually wise when a borderline diet of this type is long continued Usually one capsule or tablet containing the normal daily vitamin requirements should be given

OBESITY DIET

Breakfast	One half grapefruit or juice of one orange One slice of toast with small pat of butter or Dry cereal with no sugar or cream Milk skimmed or black coffee
Lunch	Salad without dressing Fresh fruit dessert Glass of milk
Dinner	Clear broth if desired Average portion of meat fish or chicken Two vegetables One slice of bread or small potato Fresh fruit dessert Milk

No alcoholic or carbonated beverages or eating between meals or before retiring is permissable

The patient asking What shall I do when I am invited out to dinner? may be given a few simple rules Cocktails and appetizers must be avoided Bread and potatoes should not be partaken of at the same meal — that is the patient may have one slice of bread or a small potato but not both at the same meal A small serving of the entree may be taken and a little dessert provided that at the end of the meal the individual leaves the table slightly hungry

Patients should become familiar with the caloric values of dietary items and so be able to select their foods wisely They must be taught to add caloric values and arrange their total intake so that they average the assigned number of daily calories For example if a patient on a 1200 calorie diet consumes 1500 calories during a day he must restrict food intake during the next few days so that the excess will be made up within a week The patient must learn to consider that he has just so many calories to spend each day and that the account must be balanced at the end of the week On the other hand if he is able to save a few calories one day he may enjoy a cocktail or some other delicacy another day For many patients this approach breaks the monotony of dieting

Supper As for dinner

Note You are to eat only the foods listed on this diet and no candy soft drinks pastries, cake, cookies, ice cream pudding gravy, dressing, sauce nuts, popcorn, potato chips etc If any of these foods are taken the excess calories should be made up by reducing calorie intake on subsequent days so that the excess has been compensated by the end of 1 week
Clear soups (fat free) bouillon cubes mayonnaise made with mineral oil clear tea and coffee, vinegar, saccharine may be used in the diet without counting

Suggested Day's Menu

Breakfast	*Dinner*	*Supper*
Orange juice — ½ cup	Lean meat — 3 oz	Lean meat — 3 oz.
Bread — 1 slice	Green beans — ½ cup	Baked potato — ½ cup
Butter — 1 tsp	Squash — ½ cup	Cauliflower — ½ cup
Skimmed milk — ¾ cup	Tomato salad — ½ cup	Cole slaw — ½ cup
Poached egg — 1	Fresh peach — ½ cup	Water pack strawberries — ½ cup
Coffee	Bread — 1 slice	Bread — 1 slice
	Butter — 1 tsp	Butter — 1 tsp
	Skimmed milk — ¾ cup	Skimmed milk — ¾ cup
	Tea	Tea

At other times, when the will to lose weight is strong more can be accomplished by using a simple diet outline without a strict list of foods This is particularly true in the case of the housewife who, if she has to prepare 2 separate menus, 1 for her family and 1 *for herself*, or if she causes unhappiness by making the rest of the family suffer with her diet, will be likely to discard the list and fall back into her old habits of eating, and so gain weight For such a situation another diet, called the obesity diet, is given Although simple in construction, it has been found to be very useful It contains slightly less than 1200 calories is adequate in body requirements of protein carbohydrate and fat, but should be supplemented with vitamins daily if it is to be used over a prolonged period of time It is adequate in vitamins when used for only several weeks

advised the use of diuretics such as *ammonium chloride 1 0 gm 3 times* a day, or a mercurial diuretic 1 to 2 cc intramuscularly intravenously, or subcutaneously, daily or every other day the route of usage depending on the mercurial used Ordinarily they are not necessary and not desirable

Exercise Newburgh has calculated that the average person would have to walk 36 horizontal miles to rid himself of 1 pound of adipose tissue Hence heavy exercise work or long walks do not in themselves rid the body of much weight Moreover excessive exercise increases the appetite resulting in more food intake and a maintenance of weight Short brisk walks or exercises in moderation are useful for the morale of many patients and may be prescribed

As emphasized in the beginning obesity is always the result of overeating *The only effective therapy is to reduce significantly the calorie intake* until the desired weight is attained Thereafter a diet just sufficient to maintain the newly achieved weight should be instituted and adhered to

Lipomatoses

Under this heading are included the simpler types of localized or unusual deposits of fat different from obesity and distinguished from the more complex disorders of cellular lipid metabolism grouped under the terms lipidoses and xanthomatoses

Nodular Circumscribed or Diffuse Asymmetrical Lipomatosis There is no specific treatment for these fatty tumors unless by size or location *they cause discomfort at which time they should be excised* Recurrence is rather frequent neoplastic changes in them occur rarely

Diffuse Symmetrical Lipomatosis Adenolipomatosis When limited in extent or mild in degree this should be treated as just outlined for diffuse asymmetrical lipomatosis When more extensive the measures outlined for obesity should be tried If the metabolic rate is lowered small doses of thyroid extract may be helpful

A variety of symmetrical lipomatosis known as *progressive lipodystrophy* or *Barraquer Simon s disease* is characterized by emaciation of the upper portion of the body and obesity sometimes huge of the lower half of the body There is no specific treatment available for this type

Dystrophia Adiposogenitalis (Frolich) Cerebral Adiposity In the treatment of this condition a lesion of the hypophysis or neighboring

and gives them added incentive to maintain their diet and save a few calories

Usually the appetite decreases as the food intake is lessened If it does not do so it can be curbed very satisfactorily by eating a stalk of celery or a cube of baker s bitter chocolate half an hour before mealtime It has a satiating effect and containing no sugar, adds practically no calories

Fluid intake need not be curtailed The excess ingestion of liquids, on the other hand, particularly when it too is part of the nervous habit, should be avoided

Drugs The use of supplementary drugs is condemned by the majority of authorities on the treatment of obesity It is true that most of them supply a crutch for the patient who lacks the will power to leave the table hungry Yet, where an excessive appetite fails to diminish with lessened food intake amphetamine sulfate (benzedrine) or better still d-amphetamine (dexedrine) sulfate may be permissible Although both have the same actions and toxic effects the latter is somewhat less stimulating to the nervous system Careful studies have shown that they do decrease the appetite for food and in small doses are not harmful The recommended dosage of either preparation is 5 0 mg administered half an hour to an hour before each meal With light sleepers it is best to administer the last dose not later than 4 P M Methamphetamine (Desoxyephedrine) hydrochloride in a dose of 2 5 to 5 0 mg given as recommended for amphetamine may be used if desired

Thyroid extract has no place in the routine treatment of obesity It should be used however where myxedema can be shown to exist The presence of myxedema in an obese person can be demonstrated by two calculations of the oxygen consumption in the basal metabolic rate The basal metabolic rate as calculated on the basis of the overweight and increased body surface in simple obestity is usually in the minus zone This does not indicate necessarily the presence of myxedema but is the result of the altered factors (increased body surface area and weight) in the formula for calculation If then the oxygen consumption is re calculated on the basis of what the patient should weigh normally and the body surface of the ideal weight, nearly always the reading will be in the plus zone With the presence of myxedema however upon re calculation the reading will still be in the minus zone and this will indicate that thyroid extract should be given As with myxedema alone, here too, small doses usually suffice such as 15 0 to 60 mg daily

In the water retention phase of dieting already discussed some have

DIET FOR HYPERCHOLESTEREMIC XANTHOMATOSIS

Carbohydrate 500 gm protein 55 gm fat 50 gm calories 2 670

Breakfast Juice of 2 oranges
Rolled oats — 1 sauce dish with 1 tablespoon of sugar and 1 tablespoon of butter
Muffin — 1 whole wheat with 1 heaping tablespoon of fruit jelly
Skimmed milk — 1 cup

Lunch Grape juice — ½ cup with 3 crackers
Macaroni — ¾ cup baked with ½ cup tomato sauce 1 tablespoon bread crumbs and 1 tablespoon of butter
Lettuce — 3 leaves with 2 rings of green pepper
Muffin — 1 whole wheat with 1 heaping tablespoon of marmalade
Stuffed apple — 1 medium with meringue (teaspoons sugar 2 teaspoons raisins and 1 egg)
Skimmed milk — 1 glass

Dinner Fruit juice — ½ cup with 3 crackers
Potatoes — 2 medium baked with 1 tablespoon butter
Carrots — glazed 1 sauce dish
String beans — 1 sauce dish
Muffin — 1 whole wheat with 1 heaping tablespoon jelly
Banana — 1 large with 2 teaspoons sugar

Bedtime Juice of 1 orange with 1 teaspoon sugar

The vitamins and minerals in this diet are adequate

Hypercholesteremic Xanthomatosis Secondary to Liver Disease Xanthomatous Biliary Cirrhosis Peri cholangiolitic Biliary Cirrhosis with Tuberous and Plain Skin Xanthomata The treatment for this condition is largely dietary the patient assuming the diet habits of a vegetarian Animal proteins must be restricted but such products as skimmed milk egg white (no yolks) and cottage cheese are to be allowed Since vegetable sterols are not well absorbed from the intestines all kinds of

structures should be sought for, and, if found to be unamenable to medicinal therapy, x ray or surgery should be instituted as indicated Some reduction in weight may be achieved by methods used in the treatment of obesity, however, drastic weight reduction has been found to be harmful to the health of some patients with this disorder Gonadotropic pituitary extracts may be tried to hasten sexual development

Lipidoses Xanthomatosis

Under this heading are considered the metabolic lipid disturbances of the reticulo endothelial system and histiocytes, in certain forms these are also classified under the term xanthomatosis

Essential Xanthomatosis of the Hypercholesteremic Type Hereditary Hypercholesteremic Xanthomatosis In this type of hypercholesteremia the intake of food containing animal cholesterol must be curtailed Although such a diet will not cure the disorder it will be helpful in lowering the blood cholesterol level and aid in bringing about improvement The restriction of fat alone from the diet for the purpose of preventing esterification of cholesterol has no basis in fact The restriction of fat and meat from the diet, however, should be carried out because of their content of cholesterol and cholesterol esters, and because there is less absorption of cholesterol when the intake of these foods is low The diet should be as low as possible in animal cholesterol esters but may contain cholesterols derived from plants, plant sterols are not absorbed as well from the intestines Such a diet, then, must exclude animal products such as animal fats eggs, meat and cream Vegetable foods in the diet should be cooked with fats of vegetable origin such as olive or cottonseed oil and pure margarine To obtain the best results such a diet must be followed over long periods of time Small quantities of lean meat and lean fish may be allowed once or twice a week to help in avoiding monotony An example of a cholesterol free diet for use in essential xanthomatosis is shown on the following page

Such substances as alcoholic extracts of eggplant and of artichoke leaves have been tried and found to be ineffective in lowering blood cholesterol levels in human patients Small doses of thyroid extracts, 30 to 60 mg by mouth daily are helpful if there is a lowered metabolism, in these cases it may or may not lower the blood cholesterol level and improve the symptoms of lassitude

should be largely symptomatic with emphasis on a diet low in fat and animal cholesterols Since the external secretion of the pancreas is not involved in cases of chronic pancreatitis the amount of meat does not have to be decreased significantly

Where glycosuria is present, insulin must be given as in Diabetes Mellitus After insulin therapy the glycosuria often disappears but the hyperlipemia remains unchanged

Hyperlipemia in Glycogen Storage Disease (von Gierke's Disease) and Eruptive Xanthoma In this condition there is no effective etiological therapy treatment being directed toward the predominant phases of the disease For hypoglycemia the diet should be rich in carbohydrate A diet rich in carbohydrate is also necessary when vomiting is combined with the acetonuria Glycogen storage is not increased by a high carbo hydrate diet When hyperlipemia prevails the diet should be reduced in its fat content In either event adequate protein should be provided

Choline and other lipotropic substances are of no benefit for the hyper lipemia and liver fat in this disorder Thyroid and pituitary preparations and liver extract will have no effect X ray therapy is of no use

Hand Schuller Christian Syndrome There is no specific therapy to be given in this condition Since there is no hyperlipemia or hyper cholesteremia diets low in animal fats or cholesterols are of no benefit A normally balanced diet should be given The use of desiccated thyroid is not indicated

X ray treatment has been successful for the bone lesions in some cases particularly of the skull and other membranous bones While one bone lesion is disappearing under x ray a new bone defect however may develop near by Relapse is common X ray therapy is useful also for enlarged lymph nodes but is not helpful in le ions of the skin and viscera

Gaucher's Disease There is no known effective treatment for this condition In infants the disease is uniformly fatal within 6 months to 2 years In the adult form the condition is chronic uninfluenced by diet or any drugs that have been tried Some temporary improvement may follow splenectomy A large spleen that is causing much discomfort as it sometimes does should be removed

Niemann Pick's Disease The disease is uniformly fatal and resists all forms of treatment Splenectomy x ray and radium therapy and en docrine extracts have been of no avail The patient should be given a high vitamin high caloric diet to help delay the rapidly progressing cachexia

vegetables, fruits nuts, salads, cereals, and other carbohydrates can be permitted ad libitum Lean meat and lean fish may be allowed once or twice a week The diet sample given under essential xanthomatosis of the hypercholesteremic type is applicable here

With the presence of liver damage in these patients, ample amounts of vitamin preparations should be given intramuscularly 2 or 3 times a week The administration of choline methionine, and other lipotropic substances is not of much value in this condition, since neither increased fat transport (low neutral fat in the serum) nor a fatty liver is present

Idiopathic Hyperlipemia with Secondary Eruptive Xanthoma (Occasionally Accompanied by Glycosuria and Hepatosplenomegaly), For this condition also a diet low in fat and consisting chiefly of protein and carbohydrate should be instituted Vitamins in adequate amounts should be added For this relatively new entity in the group of lipidoses a diet of 1560 calories made up of 225 gm carbohydrate, 120 gm protein and 20 gm of fat is advised Tests in patients have shown that the addition of lecithin choline inositol and methionine to the diet have not proved to be of any benefit Such drugs as thyroxin, anterior pituitary extract, and liver extract are also ineffective

The condition of idiopathic familial hyperlipemia (creamy serum) is not infrequently a cause of abdominal colic, fever, and signs of peritoneal irritation — symptoms that usually call for abdominal exploration Surgery should be avoided, however, if the diagnosis of idiopathic hyperlipemia can be established as the cause of such symptoms

Hyperlipemia in Severe Untreated Diabetes with Secondary Eruptive Xanthoma In this condition hyperlipemia has been shown to have no causal relationship to acidosis as was once thought Proper treatment of the diabetes mellitus with diet and insulin will not only control the diabetes but will also help to correct the hyperlipemia It has been found that to correct hyperlipemia it is best for the diet to be low in fat but adequate in carbohydrate and protein A diet composed of 100 gm carbohydrate, 75 gm protein and 20 gm fat has been found to be effective The insulin regulation should be carried out as described for insulin use in the section on Diabetes Mellitus If hyperlipemia and hypercholesteremia persist after proper application of diet and insulin, chronic pancreatitis may be found to be present

Hyperlipemia in Chronic Pancreatitis and Eruptive Xanthoma In this condition as in acute pancreatitis with recurrent attacks of abdominal pain, surgery should be withheld when safe to do so The treatment

CHAPTER XXXV

OTHER DISTURBANCES OF METABOLISM

Hemochromatosis Bronze Diabetes

The treatment of this condition should be entirely symptomatic The majority of patients have associated diabetes mellitus about 70 per cent of them will respond favorably to insulin treatment which should be applied as described under Diabetes Mellitus

The response to insulin treatment, however may be quite variable some cases being hypersensitive, others resistant to insulin At the same *time there is a strong tendency to acidosis For extensive hepatic involve*ment the therapy outlined under Cirrhosis of the Liver should be instituted

Prevention Large amounts of parenteral iron over long periods of time may be a causative factor in this disease and should be avoided Some observers feel that repeated transfusions may also be contributory factors in hemochromatosis

Ochronosis

There is no effective specific treatment known for this disease Any applications of carbolic acid or picric acid to these patients should be avoided *In the congenital forms particularly* and in other forms as well it may be useful to reduce the dietary protein in half giving 0 5 gm per kilogram of body weight per day It has been suggested that the proteins low in tyrosine and phenylalanine content be particularly supplied in the reduced diet

The treatment of the joint symptoms should be carried out as outlined *under Osteo arthritis*

Porphyria

Treatment consists in measures for the management of the two types of this condition (1) the photosensitive type and (2) the intermittent type

In the *photosensitive or congenital type* of porphyria the most that

BIBLIOGRAPHY

Disturbances of Fat Metabolism

1 STRANG J M Satiety as a Factor in Nutrition States Observations on Mass Exchange *Am Jour Med Sc*, 1951, ccxxi p 537
2 THANNHAUSER S J Lipidoses Diseases of the Cellular Lipid Metabolism," *Oxford Syst Med*, 1949, iv, p 214 (3)

the treatment of acidosis for as long as the kidneys possess selective excretory ability the amount of necessary radical — in the case of acidosis this is sodium — will be retained Whether glucose bicarbonate or lactate needs to be given depends again on the disease process in which acidosis has developed

Under the general measures of treatment the routes of fluid administration and the precautions against circulatory collapse should also be considered

In severe acidosis fluids need to be replaced rather rapidly hence the saline and/or glucose solution should be given intravenously It may be given as rapidly as 1 000 cc or more per hour If tolerated fluids should be given by mouth at the same time When alkali such as sodium bicarbonate is indicated it should be given by mouth when possible to do so On the other hand sodium lactate (⅙ molar) is very effective in the treatment of acidosis and is to be administered intravenously In less urgent cases the saline or glucose solution may be given subcutaneously

In the presence of circulatory collapse the administration of whole blood or plasma by transfusion is of first importance This should be followed at once by water and electrolytes Digitalis as discussed under cardiac failure should be given only when there is evidence of heart failure

Although acidosis may occur under many circumstances severe acidosis of clinical importance is seen chiefly in vomiting diarrhea diabetes and renal insufficiency to be considered in the following paragraphs

Acidosis from Vomiting Acidosis resulting from vomiting is seen particularly in the cyclic vomiting of children Such acidosis occurs in adults also but not as frequently Circulatory collapse often becomes a problem and if it occurs should receive immediate therapy with transfusions of whole blood and plasma In addition to large amounts of sodium chloride in the form of physiological saline solution it is well to give sodium lactate and glucose also The former is to be given intravenously in the form of ⅙ molar sodium lactate 25 cc per kilogram of body weight or in the forms of lactated Ringer s solution U S P 1000 cc or 40 to 60 cc per kilogram of body weight The glucose should be given intravenously as a 5 per cent aqueous solution in 1000 cc amount this should restore glycogen store and reduce ketone production In contrast to diabetes in this form of ketosis it is not usually necessary to use insulin To restore serum bicarbonate levels some also

may be accomplished is protection from light Ordinary window glass does not filter out the exciting light, but this may be accomplished by such measures as dark glasses, umbrellas, and gloves, the body should be covered with clothing as much as is reasonably comfortable

In the *intermittent type*, acute or chronic, with abdominal or nervous manifestations careful search should be made for the prior or present ingestion of lead or of barbital derivatives in any form All barbiturates must be avoided For the abdominal symptoms warm baths and warm saline enemas should be given to aid relaxation of intestinal spasm Calcium is believed to form insoluble salts with porphyrin, and this mechanism may remove some of the porphyrin from the circulation For severe abdominal pain one of the calcium salts, calcium lactate, calcium gluconate or calcium chloride 1 0 gm. dissolved in 10 cc. distilled water, may be tried, given slowly by intravenous route (Intravenous calcium should be given with caution to any patient who has been digitalized) Crude liver extract given 5 0 cc daily by intramuscular route will probably add to improvement For intractable pain meperidine (Demerol) hydrochloride 100 mg should be given subcutaneously, if not effective morphine sulfate 8 mg should be given subcutaneously

Sleeplessness should be treated with chloral hydrate, 0 3 to 1 0 gm in iced orange juice

Surgical exploration of the abdomen should be avoided if porphyrin can be established as the cause of abdominal pain

Acidosis

Acidosis is to be looked upon not as a disease but rather as a disturbance in chemical equilibrium (homeostasis) and alteration of physiological function the treatment of which should be largely along chemical lines

Dehydration is nearly always present when acidosis of more than mild degree exists Hence the restoration of body fluids is one of the first essentials in treatment The fluid portion of the infusion is just as important as the electrolytes The fluid to be used should be given by mouth intravenously, or by rectum as indicated Large amounts may need to be given and often quite rapidly, depending on the underlying disease as discussed later

Under most circumstances sodium chloride solution in physiological strength, 0 9 per cent, is the best electrolyte solution with which to begin

should be administered parenterally either subcutaneously or intra venously Glucose solution should be given also to reduce protein wastage but it is not as important as in the treatment of acidosis When the vomiting has stopped the giving of acid sodium phosphate 1 gm every 3 or 4 hours or enteric coated ammonium chloride 4 to 6 gm a day is useful

In acute alkalosis particularly if there is severe chloride depletion ammonium chloride solution may be given intravenously It can be made up as a sterile . per cent solution to be given slowly in amounts up to 200 cc over a 4 hour period If the solution is given too rapidly there is danger of convulsions

When prolonged vomiting or diarrhea or continued drainage from a fecal fistula causes marked loss of fluid and chlorides intracellular sodium may become increased serum chlorides and intracellular potassium decreased and a high serum bicarbonate level with alkalosis may develop in order to maintain biological equilibrium If under such cir cumstances only sodium chloride and glucose are administered the patient not only may become no better but may become worse since with a high serum bicarbonate level (high CO) the kidneys will con tinue to excrete increased amounts of chloride ion with persistence of hypochloremia and alkalosis The treatment should now be directed at correction of hypopotassemia (hypokalemia) by the daily intravenous use of potassium as potassium chloride 3 to 5 gm or even more Po tassium balance should be determined by chemical and electrocardio graphic control Potassium salts should not be given or should be given very cautiously intravenously when urine output is not adequate

Alkalosis caused by Peptic Ulcer Therapy The alkalosis that may develop during antacid therapy of a gastric or duodenal ulcer is con sidered under that subject

Hyperventilation The symptoms of alkalosis seen in mild forms of hyperventilation syndrome as in anxiety neurosis may frequently be helped by making the patient conscious of the act of overbreathing and by teaching him to hold the breath repeatedly as long as possible to allow CO_2 to accumulate in the tissues The underlying neurosis should be treated properly In doing so it is helpful to use in addition a mild sedative and ammonium chloride The sedative such as phenobarbital 15 mg or chloral hydrate 0 3 gm after each meal and at bedtime may be useful in reducing the sensitiveness of the nervous system Am monium chloride 0 5 to 1 0 gm 3 times a day is helpful in maintaining

use sodium bicarbonate, 7 cc of 4 per cent solution per kilogram of body weight given intravenously Sterile solution of sodium bicar bonate for intravenous use is procurable on the market It is not to be given subcutaneously In mild cases of acidosis, in which it is desirable to use alkalis, sodium bicarbonate in 2 to 5 per cent solution can be given by mouth or by rectum

The underlying disease causing the vomiting should be treated con currently

Acidosis from Diarrhea The treatment for acidosis due to diarrhea should be carried out as outlined above for acidosis due to vomiting

In the diarrhea of infants and children some care should be exercised in the rapidity with which parenteral fluid is administered The first 300 to 500 cc may be given rather rapidly but thereafter the rate of flow should be 8 to 10 drops per minute for infants and 12 to 15 drops per minute for older children The routine administration of sodium bicarbonate solution to children is not advised As an indication for its use the CO_2 content of the blood may be used If alkali is used as 7 cc of 4 per cent solution, per kilogram of body weight, and facilities for frequent determinations of blood CO_2 content are not available, the bicarbonate administration should be stopped when the urine becomes alkaline

The underlying disease causing the diarrhea should be treated

Acidosis in Diabetes Treatment is described under diabetic acidosis and coma in the section on Diabetes Mellitus

Acidosis in Renal Insufficiency The treatment of renal acidosis is for the most part symptomatic and is outlined in the section on Chronic Nephritis

Alkalosis

Clinical alkalosis is much less common than acidosis and is seen particularly under 3 circumstances (1) high intestinal obstruction, (2) certain instances of peptic ulcer undergoing therapy with sodium bi carbonate, and (3) hyperventilation

High Intestinal Obstruction Alkalosis in high intestinal obstruction is seen particularly with pyloric stenosis in which large amounts of fluid and chloride are lost through vomiting The treatment should be di rected toward the underlying cause of the obstruction

As outlined above under the therapy for Acidosis, adequate replace ment of fluid preferably in the form of physiological saline solution

PART XIII

DISEASES OF THE ALIMENTARY TRACT

CHAPTER XXXVI

DISEASES OF THE ORAL CAVITY

Diseases of the Mouth

Acute, Aphthous and Ulcerative Stomatitis These are varities of stomatitis the ulcerative being symptomatically the most severe They are caused by a variety of conditions of general or local nature Systemic disorders avitaminoses and local irritating conditions should be corrected Local measures consist of mouthwashes and specific measures against causative agents For ulcerative stomatitis a mouthwash of 1 8000 of potassium permanganate is helpful as is a hydrogen peroxide wash prepared freshly each time by the addition of 4 cc of hydrogen peroxide U S P to a full glass of moderately warm saline solution For more markedly inflamed mouths penicillin or aureomycin should be used in a mouthwash or given for their systemic effects if infection is spreading Painful aphthae or ulcerated surface should be painted with a 5 to 10 per cent solution of silver nitrate Aphthous stomatitis may be helped by aureomycin troches If it recurs repeated smallpox vaccination is recommended With stomatitis soft bland foods are advised and usually the patient is more comfortable if he does not take alcoholic drinks or use tobacco and avoids eating or drinking anything very hot Antibiotic medication may also be causative and should be discontinued if such is the case

Parasitic Stomatitis (Thrush Soor) The mouth should be kept scrupulously clean and all feeding utensils including nursing bottles should be thoroughly sterilized Lime water or 2 per cent solution of sodium

a mild state of acidosis thus preventing the symptoms of alkalosis from manifesting themselves so quickly in some of these individuals

In the more severe and protracted cases, particularly if hyperventilation tetany ensues the patient should be made to breath into a tube or rebreath into a gas bag or should be given a mixture of 5 per cent CO_2 in oxygen In frank hysteria treatment should be carried out by a competent psychiatrist

BIBLIOGRAPHY

Porphyria

1 GOLDMAN A M and KAPLAN M H 'Acute Porphyria *Ann Int Med* 1951 xxxiv p 415
2 WATSON C J and LARSON E A 'Urinary Coproporphyrin in Health and Disease *Phys Rev* 1947 xxvii p 478

Acidosis and Alkalosis

1 GAMBLE J L Chemical Anatomy Physiology and Pathology of Extracellular Fluid *Harvard Univ Press* Cambridge Mass 1950
NEWBURGH L H *Significance of the Extracellular Fluid in Clinical Medicine* J W Edwards Inc Ann Arbor 1946
3 MOYER C A and HARRISON T R 'Changes in Fluid Balance' *Principles Int Med* Blakiston 1950 p 293
4 MASON M F and HARRISON T R Changes in Electrolyte Composition *Principles Int Med* Blakiston 1950, p 305

treated by appropriate methods described elsewhere under these several headings Recently chlorophyll has been used widely to decrease mouth and body odors It is not very effective but may be tried One tablet of the commercially available preparations 4 times a day is recommended

Diseases of the Salivary Glands

Supersecretion Salivation Ptyalism In treatment, correction of the cause is important when that is possible the cause may be a central nervous system disease such as Parkinsonism (paralysis agitans), an acute infectious disease such as smallpox stomatitis and other diseases of the mouth and throat or certain drugs such as mercury potassium iodide pilocarpine and jaborandi Not infrequently it is part of a neurosis and should be treated as such Belladonna and atropine will decrease salivary secretion these should be given in increasing dosage until an effect is obtained unless undesirable toxic reactions develop In some patients when salivation is very marked and unrelieved by other methods, removal of the submaxillary glands may become necessary

Hyposecretion Xerostomia Dry Mouth Care must be taken to keep the mouth thoroughly clean Mouthwashes especially those containing glycerine help Potassium iodide pilocarpine or jaborandi may be given with caution In some patients dry mouth is part of a neurosis and should be treated as such Often no treatment is effective

Mikulicz's Disease Treatment with arsenic iodides and x ray may cure these should be tried using liquor potassii arsenitis 0 2 to 0 3 cc 3 times a day or saturated solution of potassium iodide begin with 10 drops 3 times a day and increasing each dose by 1 drop given in orange juice milk or coffee until a satisfactory result is obtained or toxic effects appear A *trial of an antibiotic such as penicillin or aureomycin* might be effective these should be tried in usual dosage Such treatment failing radiation therapy or surgical excision is indicated

Tumors If benign and disfiguring or if malignant, tumors should be excised

Diseases of the Pharynx

Parotitis The treatment of *specific parotitis* (mumps) has been described under that heading *Non specific acute parotitis* can be prevented as an accompaniment of an acute infectious disease or as a sequel

a mild state of acidosis thus preventing the symptoms of alkalosis from manifesting themselves so quickly in some of these individuals

In the more severe and protracted cases particularly if hyperventilation tc any ensues the patient should be made to breath into a tube or rebreath into a gas bag or should be given a mixture of 5 per cent CO_2 in oxygen In frank hysteria treatment should be carried out by a competent psychiatrist

BIBLIOGRAPHY

Porphyria

1 GOLDMAN A M and KAPLAN M H Acute Porphyria ' *Ann Int Med* 1951 xxxiv p 415
WATSON C J and LARSON E A Urinary Coproporphyrin in Health and Disease *Phys Rev* 1947 xxvii p 478

Acidosis and Alkalosis

1 GAMBLE J L Chemical Anatomy Physiology and Pathology of Extracellular Fluid *Harvard Uni Press* Cambridge Mass 1950
NEWBURGH L H *Significance of the Extracellular Fluid in Clinical Medicine* J W Edwards Inc Ann Arbor 1946
3 MOYER C A and HARRISON T R Changes in Fluid Balance *Principles Int Med* Blakiston 1950 p 93
4 MASON M F and HARRISON T R Changes in Electrolyte Composition *Principles Int Med*, Blakiston 1950 p 305

culosis, can be detected the treatment should be as described under these headings If biopsy shows the ulcers to be caused by cancer, treatment with very high voltage x ray should be tried or surgical excision carried out

Acute Infectious Phlegmon of the Pharynx Angina Ludovici (Ludwig's Angina) Cellulitis of the Neck All of these very acute infections of the pharynx with various extensions into the neck regions should have hot or cold perferably hot, applications to the neck and prompt use of penicillin 300 000 to 600 000 units intramuscularly repeated at 12 hour intervals until the temperature returns to normal Surgical drainage will be necessary if there is evidence of accumulation of pus Obstruction to breathing may necessitate tracheotomy instruments needed for this should be ready and easily accessible since suffocation may develop extremely rapidly

Retropharyngeal Abscess This should be looked for very carefully whenever there is any inflammatory process in or about the pharynx When found it should be drained promptly by incision Penicillin should be given even after drainage has been instituted The possibility of obstruction to breathing should be kept in mind speedy tracheotomy may be necessary to prevent suffocation the physician should be ready to make one on short notice

Tumors of the Pharynx These will need high voltage x ray treatments or surgical excision

Diseases of the Tonsils

Acute tonsillitis has already been discussed under that heading *Suppurative tonsillitis* or *quinsy* should be treated with hot application or fomentations to the sides of the neck Pain should be controlled with codeine or morphine Hot irrigations to the posterior pharynx should be used Penicillin 50 000 units every 2 hours or penicillin procaine 300 000 units in aqueous suspension plus 100 000 units of potassium penicillin given intramuscularly 2 times a day is advised Aureomycin chloramphenicol or terramycin 2 0 gm divided into 4 equal doses may be given daily Fluctuation should be felt for and when found should be drained promptly by incision with a curved bistoury covered almost to the point with cotton Sometimes before fluctuation can be detected the tonsils become so swollen that they obstruct respiration

bicarbonate should be used to wash out the mouth after each feeding The patches should be painted with 1 per cent gentian violet in 15 per cent alcohol Permanganate of potassium 1 10,000 may also be used as a spray This form of stomatitis prevails especially in those who are in a very debilitated condition from any cause These patients need correction, so far as possible, of any underlying disease, and every effort should be made to improve their nutrition and general condition

Sore Tongue The most common causes include (1) neurosis, ( ) ill fitting dental plates (3) pernicious anemia, and (4) antibiotic therapy Syphilis and cancer are much less common The underlying cause should be carefully sought out and treated with improved dentures liver or vitamin B_{12} for pernicious anemia and proper treatment for syphilis or cancer Sore tongue from antibiotics should be treated by stopping the drug by mild mouthwashes and by large doses of thiamin chloride, 100 mg 3 times a day

Gangrenous Stomatitis (Cancrum Oris Noma) Destruction of the sore by actual cautery is the most effectual local treatment The patient has the symptoms and signs of a very severe infectious disease and should be treated with the methods described for this and given large doses of penicillin or aureomycin

Mercurial Stomatitis (Ptyalism) This is now a condition of rare occurrence The use of mercury in therapy or industrial exposure to it should be stopped immediately The mouth should be treated as ad vised earlier for severe non specific stomatitis Dimercaprol (BAL) as described for Mercury Poisoning should be used The bowels should be opened by such a cathartic as magnesium sulfate to increase the ex cretion of mercury For salivation atropine sulfate may be given hypo dermically in doses of 0 65 mg Mercurial stomatitis can be largely avoided by careful dental hygiene

Leukoplakia Buccalis Irritants such as hot foods and tobacco should be discontinued A mouthwash containing a tablespoonful of glycerine to a glass of water and 2 teaspoonsful of sodium bicarbonate makes a useful treatment for this condition X ray therapy may be helpful The lesions should be watched closely for evidence of developing epithelioma if this occurs excision is the proper treatment If it is of syphilitic origin, antisyphilitic treatment is indicated

Fetor Oris This may follow or accompany stomatitis, pyorrhea al veolaris tonsillar disease and various diseases of the nose pharynx, larynx bronchi and lungs Any of these found to be present should be

CHAPTER XXXVII

DISEASES OF THE ESOPHAGUS

Acute and Chronic Esophagitis

Treatment must be directed toward relief of the irritation If strong caustics such as acids alkalis iodides mercury and such have been taken *treatment must be directed immediately toward prevention of further* damage by the neutralization or removal of the toxic substance as described under *poisoning with these substances.*

If a severe degree of inflammation and irritation is present nothing should be given by mouth. Fluids and nourishment in the form of 10 per cent glucose solution physiological salt solution and 5 per cent purified protein hydrolysate by vein or rectum are indicated If necessary a gastrostomy should be performed and feeding given by this route until the inflammation has subsided sufficiently to permit food by mouth

As soon as possible a bland diet should be given by mouth The food should be strained and care must be taken that the patient does not eat food while it is too hot Alcohol and tobacco should be avoided Antispasmotic sedatives and swallows of a dilute alkali or antacid solution such as dilute lime water milk of magnesia, or aluminum hydroxide *may prove helpful*

Meperidine (Demerol) hydrochloride 50 to 100 mg or methadone *hydrochloride 5 to 10 mg are indicated for pain especially if the pain* is produced by spasm Penicillin streptomycin, aureomycin, or chloramphenicol as indicated by the sensitivity of the infecting organisms, should be given to control infection

In patients with chronic esophagitis a bland diet antacid therapy with aluminum hydroxide or a mixture of aluminum hydroxide and magnesium trisilicate (Gelusil) proper antibacterial therapy and mechanical

to surgical operations, particularly abdominal operations, by rigid cleanliness of the mouth and by preventing it from drying, as so often happens when the mouth stays open for more than a short time This can be accomplished by the patient s drinking water frequently and holding ice in his mouth and by spraying with a mild antiseptic solution containing a little glycerine If acute parotitis develops, an ice bag or hot compresses should be applied whichever is most comforting to the patient Penicillin or aureomycin should be given early in the usual dosage If signs of suppuration appear surgical drainage should be carried out

Sialolithiasis Salivary Lithiasis Salivary secretion should be stimulated by giving potassium iodide or pilocarpine in an effort to wash the calculus out through the salivary tract Sometimes gentle manual manipulation will move the stone along the duct Sometimes surgical excision will be necessary

Stricture or Kinks of Salivary Duct Instrumental probing and dilatation is the indicated treatment

Acute Pharyngitis Sore Throat Angina Simplex This should be treated as described under Acute Tonsillitis The early use of penicillin or aureomycin will almost always greatly decrease the duration of these inflammations and prevent complications

Vincent's Angina Penicillin seems to be the most effective therapeutic agent for this and should be given intramuscularly in a daily dose of 300 000 units of procaine penicillin in aqueous suspension Topical applications of 10 000 to 15 000 units of penicillin should also be used 4 times daily in a solution of 500 units per cc When there is accompanying pyorrhea or bad teeth dental care is indicated Good results are claimed from giving in addition to the other treatment niacinamide in a dosage of 0 2 gm 3 times a day Diseased tonsils should be removed after the acute features of Vincent s angina have been ended by the treatment just described

Chronic Pharyngitis Smokers and speakers often suffer from this When it is so caused smoking should be stopped and speaking limited For the latter, training in voice use will be very helpful Steps should be taken to improve general health change of air and scene will help in this Local treatment with sprays gargles and pastilles of various sorts will be helpful Diseased tonsils should be removed infected sinuses treated, and any diseased condition in the nose be remedied, if that is possible

Ulceration of the Pharynx If the cause such as syphilis or tuber

done by one especially trained in the technique Many patients are relieved by one dilatation After dilatation a bland diet must be continued for 4 or 5 months If peroral dilatation fails, surgery should be resorted to as a last measure

Congenital Short Esophagus

This condition often associated with herniation of the stomach through the diaphragm usually responds satisfactorily to medical therapy Treatment should be directed toward the relief of symptoms and the establishment of an adequate passageway if obstruction exists The patient should be placed on a bland low residue diet and all food should be chewed thoroughly Meals should be small and when indicated given at frequent intervals Gas forming and bulky foods should be avoided Liberal use of liquid aids in washing down food and helps prevent stagnation at herniation or stricture sites All meals must be taken while the patient is sitting erect and he must be cautioned against lying down immediately after meals Pressure on, or constriction of the abdomen must be avoided *It is wise to avoid eating for at least 3 to 4* hours before going to bed Occasionally it is necessary to sleep in a semi sitting position in order to avoid distress

Emotional excitement and physical exertion should be carefully *avoided just before during and immediately after meals*

Antispasmotics are helpful in some cases Atropine sulfate 0 4 to 0 6 mg 15 to 30 minutes before meals 3 times daily homatropine methylbromide 2 5 to 5 mg repeated at 4 hour intervals 1 hyoscyamine (Bellafoline) 0 25 to 0 5 mg or tincture of belladonna 0 6 to 1 2 cc 15 minutes before meals all given orally are recommended All of these have undesirable side reactions such as dryness of the throat rapid pulse and impairment of vision Occasionally they afford considerable relief however Phenobarbital, 15 mg 3 or 4 times a day is helpful

The anemia so commonly observed responds readily to iron therapy Ferrous sulfate 1 to 2 gm daily after meals or if a more bland preparation is desired ferrous gluconate in the same dosage is indicated

Obesity is an aggravating factor and if present weight reduction is indicated Occasionally loss of weight alone gives excellent results

If there is an ulcer or if ulcer symptoms are present an ulcer regime such as described under the treatment of gastric and duodenal ulcer is

When this happens a rubber tube should be passed into the trachea or a tracheotomy should be done. Often it is best, in these circumstances, to remove the tonsils. With subsidence of the active process and recovery from it, it is wise to remove the tonsils to prevent recurrence.

Chronic Tonsillitis. If there is evidence of actual disease in the tonsils or if there have been frequent recurring attacks of tonsillitis, the tonsils should be removed. If hypertrophied tonsils with or without inflammation are interfering with normal breathing, they should be removed. Tonsils should never be removed unless they may be serving as a focus of infection. By and large, many more tonsils are being removed than is justified by careful critical follow up studies. Certainly not every child should have his tonsils removed just because he is unhealthy and is not developing normally. Recurring colds are not an indication for tonsillectomy.

Adenoids should be removed from all children if and when there is evidence that they restrict normal breathing through the nose. Often they cause mouth breathing, especially in the sleeping child; when this occurs their removal is indicated. They also often cause some deafness by obstructing the eustachian tubes; this, too, calls for their excision.

Tumors. The occasional tumor of the tonsil should be removed unless it is a generalized or widespread tumefaction of lymph nodes. Then probably x-ray treatment with multiple sites of exposure will be more effective than anything else.

Tumors

Benign tumors such as fibromas lipomas, myomas and cysts, should be removed surgically if they are causing sufficient obstruction to produce malnutrition

Malignant tumors causing obstruction should be treated by x ray, radium or surgery as indicated in the individual case If malnutrition is present much can be gained by an early gastrostomy and adequate feeding

Ulceration

Ulceration of the esophagus is caused by various conditions and as a consequence treatment depends on the nature of the causative factor Most non cancerous ulcers will respond to a bland diet aluminum hydroxide gel or a mixture of aluminum hydroxide and magnesium trisilicate (Gelusil) and local application of 10 per cent silver nitrate Occasionally it is necessary to institute complete ulcer therapy as described under Duodenal Ulcer in order to obtain relief

Varices

Treatment of esophageal varices is not satisfactory The causative factors should be ameliorated as far as possible Cirrhosis of the liver, congestive heart failure splenomegaly and other causes should receive the treatment appropriate for the condition Patients with varices should be on bland soft diets Unusual exertion such as straining at stool coughing vigorous laughing lifting of heavy articles or anything that will bring about an increase of venous pressure should be avoided Injection of sclerosing solutions, such as 5 per cent sodium morrhuate into the varices is helpful in some cases

Various surgical procedures aimed at establishing collateral circulation have given varying degrees of relief These are the Eck fistula omentopexy anastomosis of the splenic vein to the left renal vein and the establishment of collateral circulation in the posterior mediastinum Ligation of the hepatic artery close to its point of origin may prove palliative in portal hypertension

Hemorrhage from the rupture of a varix is serious and often results

dilatation of strictures usually give good results If ulceration exists, direct treatment through the esophagoscope is indicated Application of 10 per cent silver nitrate is helpful in promoting healing in some chronic ulcers, but this must be used with great caution Infections in the mouth, nose, and throat should be eliminated

If the lesion is due to iron lack such as occurs in the Plummer Vinson syndrome the administration of ferrous sulfate or ferrous gluconate, 1 to 2 gm daily, and repeated passages of the esophagoscope give excellent results

CARDIOSPASM

After careful studies have shown what the true nature of the lesion is, treatment should begin with reassurance, since there is a large psychic factor in many of these cases and psychotherapy may give excellent results The patient should be informed that there is no organic lesion of the esophagus He should be carefully instructed to avoid emotional upsets before or during meals, food should be partaken under pleasant conditions with ample time allowed for thorough mastication Highly spiced hot cold, or rough foods should be avoided Nutrition should be brought up to and maintained at a high level Supplementary vitamins especially of the B complex, should be given Parenteral glucose vitamins, fluids, plasma albumin, amino acids and transfusions are all helpful when cardiospasm prevents adequate intake of fluids and foods Daily removal of food residue in the esophagus and lavage with warm saline solution are helpful in preparing the patient for corrective measures If a stomach tube can be passed it is most desirable to rest the esophagus and by using tube feedings build up the patient s nutrition The tense, excitable patient may be helped by mild sedation with pheno barbital If an iron deficiency anemia exists ferrous sulfate or the more bland ferrous gluconate should be given in a daily dose of 1 to 2 gm

Antispasmotics given orally one-half hour before meals, such as atropine sulfate, 0 4 to 0 6 mg, 1-hyoscyamine (Bellafoline), 0 25 to 0 50 mg, tincture of belladonna, 0 6 to 1 2 cc, or nitroglycerine, 0 6 mg, may be helpful in mild cases, but for the most part results from these are disappointing

If the preceding measures fail and no ulcer exists at the site, excellent results may be secured by stretching the spastic area with an hydrostatic, pneumatic, or mercury bougie dilator The stretching should be

CHAPTER XXXVIII

DISEASES OF THE STOMACH

Acute Gastritis

In the treatment of acute gastritis the noxious agent should be removed as quickly as possible and the stomach should be placed at complete rest by withholding food, a very gradual resumption of its function of digestion should be allowed

Since the most common cause of acute gastritis is the ingestion of a substance or substances irritating to the stomach the first step in treatment is to avoid the harmful agent Such agents may include improperly cooked foods spoiled foods articles of diet seasoned too highly and various drugs and chemicals including alcohol

The symptoms are usually acute and demand immediate action in emptying the stomach If vomiting does not occur spontaneously, the patient should be made to gag and that failing gastric lavage or even an emetic are in order With food poisoning the patient should drink mustard water 8 gm (2 teaspoonfuls household mustard) in 250 cc of water or concentrated salt solution to promote emesis If the material ingested is known not to be a corrosive a well lubricated stomach tube should be inserted and repeated lavage continued by use of a warm weak solution of sodium bicarbonate followed by repeated washings of the stomach with water until the contents return clear A purge should then be given a dose of castor oil for children 1 to 2 cc per year of age for adults 30 cc or a saline cathartic such as magnesium *sulfate 15 to 30 gm with 2 glasses of water for adults children should* receive 15 gm with 1 glass of water

In the case of poisons or corrosives taken accidentally or with suicidal intent the measures just outlined should be carried out with modifica

indicated Mild distress will usually disappear on a bland diet and on such antacids as a mixture of aluminum hydroxide and magnesium trisilicate (Gelusil) If tablets are used, they should be permitted to dissolve slowly in the mouth Sodium bicarbonate may be given

If stenosis is a complicating factor gradual dilatation will give relief This may be accomplished by passing olive-tipped bougies over a previously swallowed string Usually 3 or 4 treatments a year are sufficient When chronic ulceration exists, the application of 10 per cent silver nitrate through the esophagoscope may promote prompt healing

Surgery may not give very satisfactory results In a small percentage of cases, however it is necessary and may prove most helpful Phrenic nerve exeresis on the left often gives relief Surgical repair of the diaphragmatic opening is not usually very successful in cases of a congenitally short esophagus

Diverticulum

Diverticula or pouches leading off from the esophagus may be the result of congenital weakness of the esophageal wall, of traction from adhesions, or of pressure within the esophagus Unlike the hypopharyngeal diverticulum which always requires surgical removal, these are benign, and treatment is palliative Usually a glass of water taken after a meal will wash out the sac Patients should then lie flat for 15 to 30 minutes to insure complete emptying

Surgery is indicated if the sac becomes large or is producing troublesome symptoms

Paralysis

Paralysis of the esophagus is fortunately rare Treatment is difficult and for the most part consists of tube feedings combined with treatment directed toward amelioration of the cause

Spasmotic drugs, directed toward increasing tone and motility of the esophagus may be tried Occasionally one of the following may prove helpful acetyl-beta methyl choline chloride (Mecholyl), 100 to 200 mg orally once or twice a day, carbaminoylcholine (Doryl) 0 25 to 0 5 mg subcutaneously, or [illegible] 0 mg 2 or 3 times daily orally or neostigmine bromide (Prostigmine), 15 mg [illegible] or 3 times daily orally

Antimony Tartar emetic		Wash out stomach with large amounts of water Give by tube 15 to 30 gm of sodium sulfate Give dimercaprol (BAL) as for arsenic poisoning Keep warm Give large amounts of fluids and caffeine and morphine if necessary Atropine sulfate 0.5 to 1.0 mg repeated 2 or 3 times a day will help relieve severe cramps
Arsenic Arsenious acid Fowler's solution *Paris green* "Rough on Rats"	0.1 gm	Wash out stomach with large amounts of warm water and leave 15 or 30 gm of sodium sulfate in the stomach Dimercaprol (BAL) 3.0 mg per kilogram of body weight every 4 hours for 2 days followed by 3.0 mg per kilogram of body weight 3 times a day on the third day and then the same dose times a day for 10 days Give large quantities of fluid by mouth keep warm, and give atropine caffeine and morphine as needed to control symptoms
Copper Copper sulfate (Blue vitriol) Copper subacetate (Verdigris) Copper aceto arsenite (Paris green)	0 gm	Wash out stomach with 1:1000 potassium ferrocyanide Egg albumin every 2 or 3 hours magnesium oxide milk of magnesia Keep warm Give caffeine and morphine if necessary
Formaldehyde (Formalin)	30 cc	Wash out stomach Give egg albumin from 6 to 12 eggs urea in massive amounts and sodium sulfate, 15 to 30 gm Atropine sulfate 0.5 to 1.0 mg to control excessive secretions Artificial respiration and oxygen when necessary Morphine for pain
Iodine		Wash out stomach with starch solution or flour and water Give egg albumin and milk. Keep warm Give morphine for pain
Lead Salts Lead acetate White lead Lead oxide Red lead	5 gm	Wash out stomach Give egg albumin milk of magnesia milk sodium sulfate for catharsis. Disodium hydrogen phosphate 4 gm 3 times a day Sodium citrate 5 gm in 30 cc of water with fruit juice 4 times a day If colic is severe give 50 cc of 2.5 per cent solution of sodium citrate intravenously Atropine sulfate 0.5 to 1.0 mg subcutaneously for relief from cramps Morphine sulfate 8 mg subcutaneously for pain For chronic poisoning see Chronic Lead Poisoning under Intoxications
Mercury Mercury bichloride (Corrosive sublimate)	0.2 to 0.3 gm	Give egg albumin from 6 to 12 eggs at once Wash out stomach with 5 per cent solution of sodium formaldehyde sulfoxylate leaving 200 cc in the stomach Give dimercaprol (BAL) 3 mg per kilogram of body weight—in severe poisoning one

in death Temporary intra esophageal venous tamponade produced by means of a rubber bag attached to the end of a rubber tube and inserted into the esophagus and then inflated may prove life saving Usually the bag can be removed after 2 to 3 days, following which injection or other surgical relief measures may be employed for more permanent relief

BIBLIOGRAPHY

1 CRILE, G, Jr and ROBNETT A H "Treatment of Pharyngo Esophageal Diverticulum by Inversion of Sac, *Cleveland Clin c Quart*, 1951 xviii p 42

2 EFFLER D B and COLLINS E N Complications and Surgical Treatment of Hiatus Hernia and Short Esophagus with Thoracic Stomach *Jour Amer Med Assoc*, 1951, cxlvii p 305

3 THOREK P Diagnosis and Treatment of Esophageal Diseases ' *Jour Amer Med Assoc*, 1952 cxlviii, p 808

from food for 24 to 48 hours is necessary At the end of this period warm liquids for 24 hours followed by a bland diet for a few days are advisable *After that a normal diet may be instituted gradually*

Chronic Gastritis

The treatment for chronic gastritis in its several forms is much less specific than the treatment just outlined for acute gastritis Since the cause generally remains unknown the treatment for the most part is symptomatic with careful attention to general hygienic measures

All possible etiological factors should be removed Alcohol can undoubtedly be incriminated in some instances and its avoidance then becomes mandatory Some believe that nicotine may be a factor and so it seems wise to reduce excessive smoking as well as tobacco chewing, which is usually coupled with the swallowing of tobacco juice There are numerous adherents to a belief that discharges from nose, sinuses and teeth when swallowed into the stomach cause various forms of gastritis although there is little evidence that this is so Such infections *if present* should be eliminated however when it can be done with reasonable measures as a means of bettering general health Since adequate mastication of food is of considerable importance in the dietary regime to be carried out the teeth should receive dental care with thorough cleaning and needed treatment of cavities

If allergy to food is the cause of the gastritis the offending substance or substances should be eliminated from the diet

Dieting is the most important part of the treatment of chronic gastritis The food should be bland and nourishing frequent small feedings should be given and should be well masticated All condiments highly seasoned foods and roughage should be avoided Ice-cold and very hot drinks strong tea and coffee are capable of causing difficulty and should be withheld when they do The types of foods usually prescribed for an ulcer regime are quite satisfactory for these patients In between feedings of milk and cream crackers and alkalis are frequently of benefit In severe hypertrophic gastritis with superficial ulcerations a strict ulcer regime with hourly feedings of antacids and milk should be instituted When severe dietary restrictions need to be imposed the diet should be supplemented with oral vitamin preparations Diets suitable for use in the treatment of chronic gastritis will be found under *Duodenal Ulcer*

tions in the lavage fluid depending on the substance ingested Care must be exercised in the use of the stomach tube for if perforation of the esophagus or stomach should occur, immediate surgery would be neces sary Table 1 suggests antidotes for some of the more commonly en countered poisons

TABLE XIV

ANTIDOTES FOR CORROSIVE POISONS

Poison	*Smallest Fatal Dose*	*Treatment*
Acids Inorganic Hydrochloric Nitric Phosphoric Sulfuric	 4–20 cc 8–10 cc 4 cc	If corrosion is present, avoid the stomach tube Give milk of magnesia magnesium oxide sodium bicarbonate solution chalk egg albumin Keep warm Caffeine sodium benzoate 0 5 gm repeated as needed Atropine sulfate 0 5 mg repeated every 4 hours if cramps are severe Morphine sulfate 8 mg for pain repeated in 4 hours if needed
Organic Acetic Carbolic (Phenol) Cresol (Lysol) Creosote Guaicol Oxalic	 4–20 cc 4 cc 2–8 gm	Avoid the stomach tube. Give magnesium sulfate for catharsis Milk of magnesia lime water albumin Avoid oils alcohol or glycerine Keep warm and give artificial respiration if necessary Caffeine so dium benzoate 0 5 gm intramuscularly repeated in 15 to 30 minutes if necessary Morphine sulfate 8 to 15 mg for pain In oxalic acid poisoning cal cium must be given at once use lime water calcium chloride calcium carbonate or plain plaster from the walls if necessary Calcium glu conate or chloride, 10 per cent solution 10 cc. by intravenous injection Induce vomiting immedi ately Avoid giving salts of sodium or potassium.
Alcohols Ethyl Methyl	 100–250 cc 30–60 cc.	Wash out stomach with sodium bicarbonate solu tion Carbon dioxide inhalation—respirator if tion.Artificial respiration Oxygen inhalation—res pirator if needed Give 50 cc. of 50 per cent glucose intravenously plus 15 units insulin Keep warm. Give caffeine sodium benzoate 0 5 gm intramus cularly and repeat as needed Amphetamine sulfate 10 to 20 mg intravenously repeated in 1 hour If patent becomes violent give paraldehyde 8 to 10 cc See section on treatment of ethyl and methyl alcohol intoxication
Alkalies Lye Caustic soda Potash Ammonia Lime	 2–16 cc	Do not use stomach tube Give large amounts of vinegar lemon juice grapefruit juice milk egg albumin. Caffeine and morphine if necessary Keep warm

Surgery is not ordinarily indicated in cases of chronic gastritis If there is an associated duodenal ulcer with a pyloric obstruction not controllable by medical treatment, operation should be advised If at the same time the gastritis is localized near to, or is most marked in the vicinity of, a gastric ulcer, subtotal gastrectomy may be of benefit *Finally, if cancer cannot be ruled out, exploration is advised*

Alcoholic Gastritis

The treatment of alcoholic gastritis is described under Acute Gas tritis and Chronic Gastritis

Acute Dilatation

Acute dilatation of the stomach is seen primarily under two circumstances (1) in a post operative or post partum state and (2) with severe infections Occasionally it is also seen following injuries to the brain or spinal cord In the first instance the condition is for the most part preventable by proper pre operative care

Prophylaxis is the proper treatment of post operative gastric distention The patient with gastro-intestinal obstruction and vomiting *should be admitted to the hospital and prepared adequately with Levin* or Wangensteen tube suction and with proper fluid, electrolyte and protein balance before being taken to the operating room Cathartics and purges should be avoided During operation the stomach and bowel should be handled as little as possible After operation the position of the patient should be changed frequently and gastric intubation instituted at the first signs of distention discomfort or regurgitation

When acute dilatation of the stomach occurs after operation, continuous Wangensteen suction should be applied The patient should be allowed nothing by mouth except sips of water or chipped ice to quench the thirst. Constant suction withdraws large amounts of fluid and electrolytes, especially chlorides, which should be replaced adequately, *volume for volume with parenteral saline and added glucose solution* These may be given subcutaneously or intravenously as physiological saline, as 5 per cent glucose in distilled water or as 5 per cent glucose in normal saline At present, frequent change of the patient's position is considered of less importance but on occasions it may be useful par-

		dose of 5 mg per kilogram of body weight should be given — every 4 hours for 24 to 48 hours then the same dose 3 times a day for one day then the same dose 2 times a day for 10 days Keep patient warm Give caffeine morphine and atropine as needed to control symptoms Maintain adequate hydration and give 5 to 10 per cent dextrose solution as needed by vein if necessary
Phosphorus Rat pastes Matches	0 5 to 0 2 gm	Use copper sulfate 0 5 per cent solution to wash out stomach Potassium permanganate 1 1000 as a stomach wash is also effective Dextrose 10 per cent intravenously and calcium gluconate 10 cc of a 10 per cent solution intravenously Oxygen artificial respiration and caffeine and morphine as indicated by symptoms
Silver Salts Silver nitrate (Lunar caustic) (Fused silver)	20 gm	Give large amounts of table salt and water Egg albumin and milk as demulcents
Zinc Salts Zinc chloride Zinc sulfate	 6 gm 12–20 gm	Wash out stomach with sodium bicarbonate solution give egg albumin milk milk of magnesia. Keep warm Give caffeine atropine and morphine to control symptoms

In acute gastritis due to alcohol the treatment is similar to that just described In the case of methanol (wood alcohol or denatured alcohol) however lavage with sodium citrate solution 0 3 gm to the ounce or sodium bicarbonate, should be carried out, followed by forced feeding of milk and egg albumin

When an acute infection either systemic or local, is the cause of the gastritis, the infection should be treated promptly In the former seen commonly in the acute infectious diseases especially of children proper chemotherapy should be instituted In the latter if phelgmonous gastritis develops, surgery may be indicated

In the acute gastritis from any of the agents above, pain is likely to occur and may be severe The pain should be combatted, according to its degree with medicaments given parenterally For mild pain a hypodermic of codeine sulfate, 30 mg, is usually sufficient For severe pain a hypodermic of morphine sulfate, 8 to 15 mg combined with an antispasmodic such as atropine sulfate, 0 4 mg is effective Dihydromorphinone (Dilaudid) hydrochloride, 2 mg or meperidine (Demerol) hydrochloride, 50 to 100 mg, may be used for pain that is not very severe

To avoid the recurrence of nausea and vomiting, complete abstinence

Surgery is not ordinarily indicated in cases of chronic gastritis If there is an associated duodenal ulcer with a pyloric obstruction not controllable by medical treatment, operation should be advised If at the same time the gastritis is localized near to, or is most marked in the vicinity of, a gastric ulcer, subtotal gastrectomy may be of benefit Finally, if cancer cannot be ruled out exploration is advised

Alcoholic Gastritis

The treatment of alcoholic gastritis is described under Acute Gastritis and Chronic Gastritis

Acute Dilatation

Acute dilatation of the stomach is seen primarily under two circumstances (1) in a post operative or post partum state and (2) with severe infections Occasionally it is also seen following injuries to the brain or spinal cord In the first instance the condition is for the most part preventable by proper pre operative care

Prophylaxis is the proper treatment of post operative gastric distention The patient with gastro intestinal obstruction and vomiting should be admitted to the hospital and prepared adequately with Levin or Wangensteen tube suction and with proper fluid, electrolyte and protein balance before being taken to the operating room Cathartics and purges should be avoided During operation the stomach and bowel should be handled as little as possible After operation the position of the patient should be changed frequently and gastric intubation instituted at the first signs of distention discomfort or regurgitation

When acute dilatation of the stomach occurs after operation continuous Wangensteen suction should be applied The patient should be allowed nothing by mouth except sips of water or chipped ice to quench the thirst Constant suction withdraws large amounts of fluid and electrolytes especially chlorides, which should be replaced adequately, volume for volume with parenteral saline and added glucose solution These may be given subcutaneously or intravenously as physiological saline, as 5 per cent glucose in distilled water, or as 5 per cent glucose in normal saline At present, frequent change of the patient s position is considered of less importance but on occasions it may be useful, par

Drug therapy generally assumes a minor role in the treatment of chronic gastritis However, in some instances of the atrophic type, such as is seen in pernicious anemia or chronic iron deficiency anemia the use of liver extract or vitamin B_{12} may be specific These are to be administered as outlined under Pernicious Anemia Parenteral liver extract may be of benefit whether anemia is present or not Drugs which possibly are irritating, such as aspirin, iodides, drastic cathartics, chloral hydrate, and paraldehyde should be avoided

If achlorhydia is found to be present, the patient may be helped by the administration of dilute hydrochloric acid Most agree that to obtain the best results the dosage should be in teaspoonfuls and not in drops Dilute hydrochloric acid U S P, 4 to 8 cc in a full glass of water, should be taken with each meal The larger dose is sometimes helpful for an associated diarrhea To allay any oral discomfort or damage to the teeth this acid fluid should be sipped through a straw or glass tube and the mouth rinsed with an alkaline mouth wash after the meal Capsules of glutamic acid hydrochloride with plenty of water may be used instead of dilute HCL, but the results are not generally so good From 3 to 6 capsules should be taken with each meal

When hyperacidity is associated with gastritis, the antacid regime described under Duodenal Ulcer should be carried out

Gastric lavage may be instituted with benefit if excess secretion, exudation or desquamation are present in the stomach The tube should be passed in the morning when the patient is in the fasting state, followed by the introduction of a weak solution of hydrogen peroxide, 15 0 cc in 500 cc of warm water After several washings with hydrogen peroxide, use warm normal saline solution until the stomach washings return clear Some prefer a solution of calcium hydroxide U S P (lime water) for lavage because of its ability to dissolve mucus It is of additional benefit as an antacid in the presence of hyperacidity

For pain, moist heat should be applied to the abdomen Such drugs as salicylates, bromides, quinine derivatives, et cetera, by mouth are not well tolerated in chronic gastritis and should be avoided Codeine sulfate 30 to 60 mg, or meperidine (Demerol) hydrochloride, 50 to 100 mg, by hypodermic injection may be necessary for severe discomfort

Gastric hemorrhage rare in gastritis, should be treated in the same way as outlined under Duodenal Ulcer Unless a localized area of bleeding can be demonstrated surgery is not indicated, when there is such an area surgery may be desirable

be avoided by undertaking surgery Age of the patient need be no contraindication to surgery which will often prolong life

Before surgery is undertaken the general condition of the patient should be improved as much as possible with an attempt to build up his nutrition fluid and electrolyte balance and to correct any existing anemia which is so common in these cases — but very little time should be lost in doing this Cardiac and renal function should have proper evaluation and any abnormalities should be corrected, if it can be done quickly A soft nutritious diet should be prescribed Protein stores should be replenished and adequate glucose given Delay of operation however should always be very brief

Further palliative treatment may have to include a decision on the type of operation to be performed and measures to relieve discomfort If total resection of the lesion is not possible gastro enterostomy is still preferable to subsequent total obstruction Roentgen therapy is not helpful usually For mild discomfort due to spasm atropine sulfate 0 6 mg by mouth or hypodermically is useful Phenobarbital 15 mg orally 4 times a day may also be desirable in spite of its frequent undesirable aftereffects especially in patients past 60 For more severe pain hypo dermic injections of meperidine (Demerol) hydrochloride 50 to 100 mg or morphine sulfate 8 to 15 mg repeated as needed are advisable Methyldihydromorphinone (Metopon) hydrochloride 6 mg by mouth as often as required to relieve pain is also excellent in these cases These drugs should be used without hesitation in patients with cancer of the stomach If vomiting occurs gastric lavage with a soft rubber tubing may be helpful and dimenhydrinate (Dramamine) 50 to 100 mg may be used *With hemorrhage from a gastric cancer* surgery is the only treatment to advise unless surgical treatment has already been as thorough as the surgeon deems possible

Post-operative care requires very careful handling of the patient and his relatives from a psychological standpoint The utmost courage and sympathy are required in the treatment of patients with this fatal neo plastic disease

Other Tumors

These constitute non cancerous lesions and include adenomata and polyps Tumors that are apparently adenomata or polyps may be malignant in fact and when there is doubt or when they are causing obstructive

ticularly assumption of the prone position This is supposed to release pressure or traction of the mesenteric root and its vessels by the transverse duodenum

With the recent introduction of vagotomy for the surgical treatment of ulcer, there often occurs post-operatively a type of gastric dilatation that may be troublesome and difficult to manage Neither change of diet nor use of drugs produces much corrective effect upon it In some cases gastric peristalsis may be increased temporarily by the use of the parasympathomimetic drug urecholine in doses of 5 mg hypodermically or 10 to 30 mg orally one half hour before meals The effects of the drug last from 30 to 45 minutes For more permanent effects a gastro enterostomy may be necessary if it was not done at the time of vagotomy Gastric dilatation following vagotomy may improve somewhat with the passage of time

The treatment of acute gastric distention associated with a severe infection is carried out in the same way as outlined in the preceding paragraph with constant gastric suction proper fluid and electrolyte balance plus a vigorous attack on the infectious process In pneumonia meningitis, typhoid fever peritonitis and other infections in which this complication occurs not infrequently the proper chemotherapeutic agent should be given and all supplementary measures should be carried out as described under the respective headings of those diseases

The gastric distention occurring after central nervous system injury may require prolonged treatment with constant gastric suction and adequate fluid and electrolyte balance Ordinarily in acute gastric distention surgical treatment should play no part but the distention following nerve injury may be an exception

Cancer

The treatment for cancer of the stomach should be prompt, with complete resection of the tumor early in the course of the disease Such is the ideal but unfortunately the disease is too often far advanced, with metastases and manifestations of malnutrition anemia and, perhaps obstruction when it is discovered Even in the seemingly more advanced cases surgery should be undertaken for it is difficult to be sure of extent except by direct inspection enlarged lymph nodes may be inflammatory, and death from obstruction with its symptoms would

aid further in relieving the epigastric distress Phenobarbital, 15 mg by mouth 4 times a day may help, if undesirable aftereffects are not too great The patient with such a herniation can continue to lose small amounts of blood and this may lead to severe secondary (hypochromic) anemia This can be best treated with iron either ferrous sulfate or ferrous gluconate 0 3 to 0 6 gm 3 times a day On the other hand severe and recurrent hemorrhage is an indication for surgical treatment Some believe that the pain and particularly the bleeding are always due to an ulceration of the lower end of the esophagus This should be treated in the same manner as has been outlined for the medical treatment of Duodenal Ulcer In the vast majority of cases however distress and even the bleeding is due to congestion of the mucosa of the lower end of the esophagus. When ulceration is present, the local application of 10 per cent silver nitrate to the ulcer through an esophagoscope will be beneficial in promoting healing

Hematemesis

Of the many causes of hematemesis from involvement of the arteries or veins of the stomach by far the most common are ulcer gastric cancer and cirrhosis of the liver with esophageal varices The treatment of hemorrhages from these sources is considered under their respective headings The treatment of hematemesis from other causes is considered under the various causative conditions

Neuroses

This group of stomach disorders does not represent a disease or even a symptom complex, for there is the greatest variety in the clinical picture, not only in the comparison of one patient with another but in the same patient from time to time

The treatment of the wide variety of symptoms that may be presented may vary from very simple to rather complex procedures but of first importance is careful examination followed by repeated examinations to rule out organic disease of the stomach gall bladder, appendix or kidneys as the cause

symptoms, they should be removed. Benign adenomata and polypi, as seen in achylia gastrica and occurring rather frequently in the stomach of patients with pernicious anemia, do not usually require surgical removal.

Foreign Bodies

When symptoms are caused by the presence of a foreign body, or the potentiality for symptoms and complications exists, as with a sharp point, the object should be removed. All foreign bodies that cannot be passed by the rectum should be removed surgically.

Hypertrophic Stenosis of the Pylorus

After proper pre-operative preparation with the correction of dehydration, acidosis or alkalosis, the treatment for hypertrophic stenosis of the pylorus should be surgical. Mortality from the disease is low when treated by a surgeon experienced in the management of the very young, in whom this condition is usually found. Careful parenteral feedings with gradual resumption of oral food is important after operation.

Diaphragmatic Hernia. Esophageal Hiatus Hernia

When diaphragmatic hernia is associated with an esophagus of normal length or nearly normal length so that the esophagus extends to the level of the diaphragm, surgical correction may be carried out successfully. If, on the other hand, it can be established that a larger portion of the diaphragm leaf is absent, or that the esophagus is a congenitally short one, surgery is less successful. The latter is discussed on page 469.

The medical treatment for a small hiatus hernia, which requires no surgery or which precludes surgery, should consist of small, frequent feedings of bland, easily digestible foods. For the "heart burn" that may occur when the patient lies down with acid gastric juice regurgitating into the lower esophagus, antacid powders administered as in peptic ulcer, will often give relief. It is also helpful for the patient to sleep with his head elevated on 2 or 3 pillows or with blocks under the legs at the head of his bed. Antispasmodics such as atropine sulfate 0.4 mg. may

Cardiospasm may require prolonged and sometimes energetic therapy A soft liquid diet, as tolerated by the patient should be given and followed by sedatives and antispasmodics The patient should be placed at bed rest in quiet surroundings At first the drugs should be given parenterally for when retained in the esophageal dilatation they are not absorbed Sodium phenobarbital in subcutaneous doses of 0 1 gm with atropine sulfate 0 6 mg hypodermically may be tried, doses may be given as frequently as every 4 hours As the cardiac opening becomes patent, the same or similar drugs may be used by mouth Usually this treatment is not very effective To hasten improvement and to prolong results it is often helpful to dilate the cardiac orifice with dilating bougies introduced along a swallowed thread Splitting of peri esophageal fibers of the diaphragm by surgery may be necessary but results have not been very satisfactory In any patient with a large esophagus dilated from cardiospasm the possible development of a pulmonary abscess from overflow from the esophagus into the bronchial tree must be kept in mind and if it occurs should be treated as outlined under Lung Abscess

Anorexia Nervosa The treatment of anorexia nervosa requires first its differentiation from Simmonds pituitary cachexia which may be very difficult In the therapy of anorexia it is best to obtain the services of a psychiatrist for the causative mental conflict may be deep seated and requires careful analysis The remainder of the treatment is medical and consists of getting the patient to eat an adequate well balanced weight-gaining diet Any reasonable means to that end are justified Tube feeding may have to be instituted with the use of small doses of regular insulin units 5 to 10 before each meal to aid in stimulating the appetite Sometimes prolonged feedings through a nasal catheter are effective with bettered nutrition anorexia lessens and return to oral feeding becomes possible Improvement may be hastened particularly if there is low 17 ketosteroid excretion in the urine by adrenal activation through the use of corticotropin in small doses 10 mg 4 times a day for 7 to 14 days With this treatment and additional psychotherapy some patients with anorexia nervosa have shown an immediate increase in appetite and over all clinical improvement

Gastric Ulcer

The treatment for this condition is described under Duodenal Ulcer Vol VIII 353

Attention must be paid to the patient as a whole and not just to the stomach symptoms The entire condition of the patient should be made as good as possible When it has been determined that the symptoms are due to a functional derangement of the gastro intestinal tract, therapy may need to be directed against such disturbances as abnormalities in secretion derangements of motor function, pain, nausea, and vomiting, it is preferable, however, to treat the gastric symptoms as part of a neurosis and to use methods recommended for that

Disturbances of secretion may be in the form of hypersecretion, hyperacidity, or hypoacidity

Hyperacidity and *hypersecretion* generally occur together For them digestive stimulants such as alcohol should be avoided A bland type of diet high in protein and low in carbohydrate, and the use of antacids as outlined for the treatment of Duodenal Ulcer, are useful Patients with this condition are often tense and nervous, and a mild sedative such as chloral hydrate, 0 3 gm well diluted in milk or fruit juice 3 or 4 times daily, or possibly phenobarbital, 15 mg 4 times a day, is useful To these may be added atropine sulfate, 0 4 mg, taken 30 minutes before meals With continued hypersecretion gastric lavage with the stomach tube is of much value The use of surgery to reduce hyper acidity and hypersecretion should be weighed most carefully lest it begin a train of surgical operations in these often psychoneurotic in dividuals, as a rule surgery is inadvisable

In *hypoacidity* overfeedings should be avoided The diet should be easily digestible of the usual variety with adequate fruits and vegetables Alcohol is not often well tolerated by these individuals and, when this is true should be avoided Bitter tonics before meals are sometimes of value Dilute hydrochloric acid U S P in water sipped through a glass tube with the meals, can be very helpful A dose of 2 to 10 cc well diluted with water and followed by a neutralizing alkaline mouthwash, is advised Hypoacidity is often symptomless and does no harm

Aerophagia with normal or abnormal secretion can usually be treated quite successfully Explanation to the patient that air is being swallowed and then regurgitated should begin the therapy Treatment should be that recommended for a general neurosis rather than some form of gastric therapy Atropine sulfate 0 4 mg 3 times a day is often helpful A tea spoonful of equal parts of tincture of valerian and tincture of asefetida may aid in preventing recurring eructations because of the disagreeable taste when this mixture is regurgitated

ance of complications, the patient need not be hospitalized since at home all treatment except surgical can be carried out, and the latter is not usually needed

In most instances the typical post prandial pain requires the most attention Dietary principles should be directed toward adequate nourishment with frequent small feedings of foods consisting mostly of protein and fat and including vitamins in adequate amount Mechanically and chemically irritating foods foods that stimulate gastric secretions foods containing rough fibers and sharp seeds condiments, coffee and alcohol should be avoided The purpose of frequent feedings is to continue neutralization of the acid gastric juice for whether full or empty, the stomach is never completely quiet and continues to secrete acid Tobacco because it stimulates gastric secretion, should be forbidden. It is in these patients with their nervous driving make up that smoking to excess is often common and hence the avoidance of tobacco becomes an important part of treatment Alcohol if limited to a single drink and that immediately preceding the larger evening meal may be tolerated without harm After-dinner and evening drinking must not be allowed

Acute Ulcer

An acute ulceration of the lower third of the esophagus should be treated in the same manner as a duodenal ulcer An acute ulcer in the stomach requires frequent questioning about symptoms continuing x ray examination and if there is any suspicion of malignancy gastroscopy to be certain that it is a benign lesion which heals completely and is not an early neoplasm When the condition appears to be ulcer the treatment is medical with the patient in bed for 2 weeks on a Sippy regime as outlined for Chronic Ulcer followed by x ray re examination If some healing is in evidence medical treatment should be continued for 2 more weeks If none is detected surgical removal should be advised If healing is taking place strict medical treatment should be continued for 2 more weeks Then x ray re examination should be made If at this time the lesion is not completely healed or nearly so surgery should be carried out Ulcer in the duodenum is rarely of malignant nature and consequently medical management with less frequent re examination by x ray is in order

Not infrequently a patient presents the typical clinical symptoms of

CHAPTER XXXIX

DISEASES OF THE DUODENUM

Duodenal Ulcer

This is the most frequent disease of the duodenum In the treatment of duodenal ulcer it is advantageous to look upon the condition as a form of constitutional disorder in which the ulceration is but one local manifestation of disease Its occurrence in certain constitutional types, i e apprehensive and worrisome people, often with very improper feeding and living habits demands correction of many factors besides the gastric hyperacidity and the relief of pain Such factors include psychic tension, menopausal tension anemia, infections, metabolic disturbances, endocrine abnormalities such as hyperthyroidism and hypothyroidism, allergy poor nutrition, constipation, et cetera

Ulcer, whether in the esophagus stomach, duodenum, or jejunum is a chronic disease with remissions and relapses which therefore requires in treatment a constant vigilance of certain habits, particularly dietary, for adequate control of symptoms and prevention of complications In some the symptoms occur or become aggravated solely during the spring and fall months of the year in such individuals symptoms can be anticipated with efforts concentrated toward their control

The treatment of ulcer involves adequate rest of mind and body, certain principles of diet, and neutralization of excessive acid, the relief of associated spasm, and the prompt attention to complications, particularly hemorrhage, obstruction or perforation

Except for the occurrence of complications, most patients with symptoms of duodenal ulcer should be treated on an ambulatory regime In these better results may often be obtained by having the patient spend the first week or two of treatment in bed for the mental and physical rest already mentioned and to learn the principles of diet Even when the distress is protracted with nausea and vomiting or with the appear

The roentgenologist's examination is most important in the disclosure of an acute, post operative jejunal (marginal) ulcer Its presence must be differentiated from the duodenal ulcer for which the operation was done its treatment in the light of present opinion may require vagotomy The symptoms of jejunal ulcer may remain intractable and most difficult to control in this event the regime outlined for Chronic Ulcer should be carried out in detail preferably with the patient in bed in a hospital

Chronic Ulcer

The treatment for the usual case of chronic ulcer whether it be in the esophagus stomach duodenum or jejunum is primarily medical with the principles of rest, proper diet, antacids antispasmodics and proper living habits carried out over a long period of time It should be emphasized that duodenal or gastric ulcer is usually a chronic disease with the tendency to recur the individual must therefore be taught that he has to be careful for the remainder of his life of what he ingests into his stomach and he should learn early to carry out his treatment at home

In beginning treatment of a chronic duodenal ulcer gastric analysis has more than diagnostic value Once a question for much debate more and more it is being thought that the acid gastric juice bathing the ulcer, is an important cause of the ulcer pain and of retarded healing leading to chronicity For that reason gastric acid should be buffered in the treatment of an ulcer and unless measurements of gastric acidity are made neutralization of acid in treatment is purely a guess It is well known that gastric acidity varies from time to time, yet a gastric analysis done carefully after histamine stimulation gives one some conception of what the stomach can do under stress and at the same time it can act as a guide to what buffer therapy — little moderate or intensive — needs to be carried out Success in ulcer management depends largely on maintaining as continuously as possible a very low grade of gastric acidity anacidity if possible

Diet A diet proper for ulcer disease should be one that will aid in buffering gastric acidity that certainly will not provoke more acid secretion that is smooth and not rough and one that provides adequate calories minerals and vitamins Protein and fat usually predominate in the best ulcer diets because they buffer gastric acidity better than carbohydrates Another essential in such a diet is frequent feeding since

ulcer, but x-ray fails to reveal any ulcer and may or may not show irritability of the duodenal cap The ulcer may be acute and shallow with only an erosion This happens much more frequently with duodenal than with gastric ulcers Although the first x ray studies do not demonstrate a lesion, repeated examination of such patients will often show increased acidity as seen in ulcer disease, prompt response to ulcer treatment and, later the development of a characteristic niche or deformity of chronic duodenal ulcer For these reasons such cases, appearing to be instances of acute duodenal ulcer, should be treated in the same way as outlined for chronic ulcer

In this connection a word should be added concerning the criteria of activity or inactivity of an ulcer It is our opinion that, when symptoms such as pain, nausea, and vomiting are present, when there are evidences of obstruction, or when signs or symptoms of bleeding are found the ulcer is active regardless of what the roentgenograms show We do not believe that the roentgenologist from the objective evidence of a crater alone can tell whether an ulcer is active or inactive, these terms should have a clinical rather than x-ray connotation We have seen many cases of duodenal ulcer in which x ray studies were normal because of the superficial character of the lesion, because of its location, or because of bleeding that had filled the ulcer with clot, in which activity was present and treatment directed toward an ulcer was successful Likewise a crater readily demonstrable by x ray may be called active when there are no signs or symptoms of disease and the ulcer is a healed one

Based on these premises, strict ulcer therapy should be carried out whenever there is clinical evidence of activity, it should be left to the roentgenologist to determine the site of the lesion Even in the presence of pyloric obstruction associated with ulcer, the roentgen ray interpretation may require modification since the patient may vomit large amounts of long-retained food — indicating obstruction — and flouroscopic examination may reveal the free passage of barium through the pylorus Conversely barium in the stomach may show a large retention, when clinically the digestive processes are being adequately performed All this is not to detract in the least from the importance of roentgen ray examination of the upper gastro intestinal tract but to point out that not too much reliance should be placed on the x-ray examination in the treatment of ulcer, as is being done more and more with the increasing expertness of the roentgenologist s examination

5th Day	3 ounces milk and cream hourly 7 a.m.–9 p m 1 egg at 12 noon and one egg at 5 p m
6th Day	3 ounces milk and cream hourly 7 a m.–9 p m 1 egg at 12 noon and one egg at 5 p m 3 oz cereal at 7 a.m. feeding
7th Day	3 ounces milk and cream hourly 7 a m –9 p m 1 egg at 12 noon 5 p m and 9 p m 3 ounces cereal cream of wheat farina at 7 a m
8th Day	3 ounces milk and cream hourly 7 a m –9 p m 3 ounces fine cereal at 7 a m and 3 p m. 1 egg at 9 a m and 5 p m
9th Day	3 ounces milk and cream hourly 7 a m –9 p m Same as eighth day plus egg at 8 p m
10th Day	*3 ounces milk and cream hourly 7 a m –9 p m* 3 ounces fine cereal at 7 a.m. 11 a.m and 3 p m 1 egg at 9 a m 5 p m and 8 p m

Tenth Day to Third Week

Same as tenth day with a small piece of toast with butter added at 11 a m and 1 3 and 5 p m

Third Week

7 a m	Juice of one orange strained oatmeal with cream 1 slice of toast 6 oz milk and cream
9 a m	1 soft cooked egg 1 slice toast 1 teaspoon preserves *6 oz. milk and cream*
11 a m	1 raw egg with 6 ounces milk and cream
1 p m	1 serving mashed potatoes with butter 1 slice toast 6 ounces milk and cream
3 p m	Tapioca pudding with cream 1 slice toast 1 soft cooked egg 6 ounces milk and cream
5 p m	1 egg with milk prune souffle 1 slice toast
7 p m	Cream of wheat with butter applesauce 6 ounces milk and cream
9 p m	1 soft coddled egg 1 slice toast, 6 ounces milk and cream
10 p m	½ glass orange juice (may be diluted if necessary)

the stomach and duodenum are never quiescent, and having a small amount of easily digestible food material constantly in the upper gastro-intestinal tract has been found to be helpful in neutralizing acid, relieving pain, and healing the ulcer Some prefer the dietary treatment of ulcer to be progressive, that is, to begin with hourly feedings of liquids and soft foods, to progress gradually to solid foods with 3 meals daily and between meal feedings coincident with improvement Such a diet is recommended when bed rest is instituted, but it is not essential for ambulatory treatment Others use a modified diet, somewhat less strict in its outline In both dietary regimes rather large quantities of milk are used, since volume for volume milk will neutralize a 0 3 per cent solution of hydrochloric acid

Two diet lists are attached for use in beginning treatment in uncomplicated ulcer disease where pain is the chief manifestation, but obstruction, gross hemorrhage, or perforation are not present These complications will be considered further on Diet number 1 is the progressive type of diet, usually called the Sippy regime, for use with patients at bed rest Diet number 2, called the modified Sippy diet, is for use in treating ambulatory patients

Obese patients and individuals who are rapidly gaining weight on the milk and cream regime should be given the less fattening, skimmed milk powder (Starlac) Four ounces of this powder added to 1 quart of water makes a palatable milk preparation much less fattening than milk or cream If more buffering is needed, 8 ounces of powder to 1 quart of water makes a preparation similar to evaporated milk The added protein is nutritious, affords good buffering, but is less fattening than cream

Diet No 1

PROGRESSIVE SIPPY DIET

First to Tenth Day

1st Day	½ ounce each of milk and cream hourly 7 a m–9 p m
2nd Day	3 ounces of an equal mixture of milk and cream hourly 7 a m–9 p m
3rd Day	Same
4th Day	3 ounces milk and cream hourly 7 a m–9 p m 1 egg soft boiled at 12 noon feeding

Other foods which may be eaten

Zwieback farina corn meal or strained rolled oats
Broths bouillon chowder
Sweet potatoes hominy noodles macaroni or spaghetti cooked soft with a little cream or cheese sauce
Baked bananas
Simple puddings custard ice cream plain cake

Foods to be avoided

All sour foods chocolate pungent fruit juices and tea
Cantaloupe and melons, smoked or canned fish
Spinach salads, rough green vegetables unless vegetable puree
Sugar in concentrated form
Alcohol

Antacids The use of antacids to supplement diet in buffering acid gastric juice is helpful in the treatment of ulcer provided the antacids used do not ultimately stimulate the stomach to produce more acid Such is the feeling among many concerning the use of such alkalis as sodium bicarbonate as advocated by Sippy Yet experience has demonstrated that a mixture of 2 0 gm of sodium bicarbonate and 0 6 gm of calcium carbonate (Sippy day powder) is one of the best remedies for ulcer pain Since such a mixture tends to cause constipation antacids used in the evening hours may be prescribed as a mixture of 0 6 gm sodium bicarbonate and 0 6 gm calcined magnesia (Sippy night powder) Sippy powders should be used in the initial treatment of ulcer pain but continued use is not recommended by some physicians since prolonged administration may result in counter hypersecretion of hydrochloric acid and/or a disturbance in the acid base equilibrium in the blood serum This is particularly true in older patients Other physicians however continue the use of these powders with good results In the presence of some pyloric obstruction or impairment of renal function Sippy powders should not be continued for long When gastric acidity as measured by gastric analysis is not excessive and no more than 5 or 6 powders a day are necessary for control harm does not usually result from their continued use Sippy day powders should be given in hours alternating with the feedings of mixed milk and cream in addition to as much of the calcined magnesia and sodium bicarbonate mixture (Sippy night powder) as is needed to prevent constipation

Fourth Week

6 a m	½ glass orange juice
7 a m	7 ounces milk and cream
8 30 a m	Well cooked cereal with sugar and cream, 1 spoon applesauce, 1 poached egg on toast, glass of milk and cream
11 a m	Glass of milk and cream
12 30 p m	Very tender meat or fish, baked or mashed potato with butter toast, tapioca pudding with milk, glass of milk and cream
3 p m	Glass of milk and cream
5 p m	Glass milk and cream toast with butter and preserves
6 30 p m	Soft cooked egg fine cereal with butter 2 slices toast plain rice pudding glass milk and cream (or Jello or baked apple no skin)

Diet No 2

MODIFIED SIPPY DIET

Breakfast
½ glass orange juice sweetened, or some strained fruit
Cream of wheat or not rough" cereal
Slice of toast butter and jelly
One egg boiled or poached
Glass of milk

Lunch
Baked or mashed potato with butter, toast
Oysters or dish of very tender meat(scraped — beef, lamb veal chicken but no pork)
Cream of vegetable soup
Cup custard junket blanc mange, jellies made of gelatine

Dinner
Same as for lunch or
Soft boiled egg
Cream of wheat with butter and cream
Two slices of toast
Strained vegetables
Rice pudding (no raisins) with cream
Orange jello with cream or baked apple
Glass of milk and cream

The synthetic anion exchange resins particularly the one known as polyamineformaldehyde resin (amberlite IR 4 particle size 200 mesh) exhibit some acid neutralizing effects with no untoward side reactions when given in a dose up to 30 gm daily They should be administered in doses of 2 0 to 6 0 gm per day depending upon the level of acidity to be neutralized In the experience of the authors however they have not proved very satisfactory and until more experience is gained with them they are not recommended

Antispasmodics Spasm of the musculature surrounding the ulcer is considered to be as much a factor in pain production as the presence of free acid For that reason it is well to prescribe almost routinely an antispasmodic of which the belladonna alkaloids are best Many prefer tincture of belladonna because since it is a liquid the dosage can be regulated easily to meet the requirements of the particular patient Begin with 5 drops 3 times a day and increase 1 drop per dose per day until symptoms are relieved or until severe toxic symptoms such as dry mouth blurred vision or urinary retention develop If the dosage produces the latter the amount should be reduced by several drops if maintenance doses are to be continued It is useful to give the belladonna just before meals If tablets are to be used atropine sulfate 0 4 to 0 6 mg 3 or 4 times a day is suggested With severe spasm with any evidence of obstruction whether vomiting is present or not atropine sulfate 0 4 to 0 6 mg should be given subcutaneously Quite often perhaps due to improper absorption belladonna given orally will seem to be ineffective then the hypodermic route should be used When administering large or continued doses of atropine sulfate great care should be exercised in patients with glaucoma or with prostatic obstruction

Another but more expensive preparation l hyoscamine (Bellafoline) is also effective when administered in a dose of 0 5 mg 3 or 4 times a day or as a 1 2000 solution 20 drops 3 times a day It may also be given as a suppository containing 0 5 mg 3 times a day

Many prefer to combine phenobarbital with atropine sulfate for such antispasmodic effect and there are numerous tablets of such a combination on the market Most of them contain about 15 mg of phenobarbital and 0 3 or 0 4 mg of atropine sulfate or one of its derivatives which may be given 3 or 4 times a day Such preparations may be helpful at bedtime to prevent night pain Phenobarbital often gives undesirable after effects however especially in older patients and hence caution is needed in its use Continued use of phenobarbital is undesirable It is better

For excess secretion particularly at night the use of the continuous milk drip is recommended This may be given as plain whole milk or with 5 0 gm of sodium bicarbonate added to each quart of milk When it is used continuously over the 24 hour period, administered through a nasal tube into the stomach at a rate of 30 to 40 drops per minute, the patient receives about 3 quarts of milk and if alkali has been added, 15 0 gm of sodium bicarbonate each day Depending upon the severity of the case the milk drip type of management may be effective, particularly for nocturnal distress if instituted only from 8 P M to 8 A M, 1 quart should be used in this interval Aluminum hydroxide gel 25 per cent suspension given by continuous drip through a nasal tube at the rate of 20 drops per minute for a total of 1½ liters per 24 hours, is also helpful in controlling high acidity associated with severe pain The continuous drip is contraindicated in the presence of pyloric obstruction

Other antacids particularly calcium carbonate, the tribasic phosphate of calcium and magnesium, colloidal aluminum hydroxide, and synthetic resins have taken preference in some clinics over the use of sodium bicarbonate in the treatement of chronic ulcer None of them is as effective as the Sippy powder in neutralizing gastric acidity and giving immediate relief of pain but they are safer to use over prolonged periods of time in some patients

Calcium carbonate does not significantly disturb electrolyte balance and there is no increased tendency for renal calculi formation It is constipating but this can be corrected by administering magnesium carbonates as needed Hourly doses of 2 0 to 4 0 gm maintain the stomach at pH approximately 4 0 and when supplemented with atropine sulfate medication at about pH 5 0 both levels are excellent

Colloidal aluminum hydroxide and aluminum phosphate gel have become widely used particularly in the continuation treatment of chronic duodenal ulcer An especially desirable preparation consists of a mixture of aluminum hydroxide and magnesium trisilicate (Gelusil) Dispensed as a thick, tasty suspension such a mixture is preferred by many patients to a powder suspension in water Such gels will lower gastric acidity and are practically devoid of side reactions except that in large doses they may delay the emptying time of the stomach, particularly if pylorospasm is present The dosage to be used is 15 cc 1 tablespoonful or in tablet form, 4 tablets, at 2-hour intervals except when between meal feedings of milk or cream are being taken The tablet form is much less efficient and should not be used in the acute phase of ulcer management

become constipated this should be managed by the usual methods recommended for the treatment of constipation Force of urination will not infrequently be decreased and this indicates decreased dosage of the drug With increased usage other untoward effects some of which may be serious even fatal may appear and such possibilities require the utmost care in the administration of the drug with prompt cessation if any more than mildly toxic effects develop

More prolonged observation of large numbers of ulcer patients will be needed before methantheline (Banthine) bromide can be recommended for general use The necessity for parenteral dosage given so often throughout the 24 hours over many weeks is obviously a serious limitation to its general use When the oral administration in the same dosage produces the desired results this limitation of the drug may be obviated It would seem that for the occasional ulcer patient not helped satisfactorily by methods described in previous sections it may be helpful

Prevention of Ulcer Symptoms The following rules may be given to the patient to aid him in the prevention of recurrence of ulcer symptoms

INSTRUCTIONS FOR PATIENTS WITH HEALED ULCER

Under certain circumstances ulcer can recur in persons who are subject to this disorder You can reduce the chance of such recurrence however by following these simple rules

1 Stick to your diet If you wonder whether or not a certain *food is allowable ask your doctor Do not test foods to* determine whether they cause symptoms

2 Drink a glass of milk regularly halfway between meals and at bedtime You may take a simple cracker with the milk if you so desire

3 Your ulcer is particularly likely to recur
   a in the spring and fall
   b when you have a cold sore throat or cough If you take medicine for any of these ailments be sure to take it with milk
   c when you are physically fatigued or doing more than your usual amount of work
   d when you are emotionally upset or more irritable sleepless or nervous than usual

to give the drugs separately so that the proper dose of each can be adjusted for the patient

With the alleviation of signs and symptoms of ulcer after the successful institution of the regime above it becomes a question how long such therapy needs to be continued Often the patient with ulcer disease soon after the symptoms have been relieved neglects his diet and eating habits forgets the importance of rest and tranquillity, resumes smoking and drinking and as a result has a prompt recurrence of his trouble As pointed out in the beginning of this chapter duodenal ulcer is a chronic disease, and the patient must be taught this He must always be careful what he ingests The antispasmodics may be reduced and then discontinued soon after all symptoms and signs of spasm have disappeared The antacids must be kept up for many months, perhaps not as strictly as in the initial treatment but after meals between feedings and at bedtime when the gastric acidity is appreciably elevated The type of diet — easily digestible foods with the avoidance of roughage — must be continued indefinitely These aim at prevention of recurrence for which no specific measures are known at the present time Further in prophylaxis it has been found that prevention or proper treatment of acute infections, especially respiratory ones, the avoidance of emotional upsets and the control of fatigue are important measures in delaying even in preventing relapse

Anticholinergics Spasmolytics A new drug methantheline (Banthine) bromide has an active anticholinergic spasmolytic action that reduces gastric motility and frequently decreases the volume and acidity of the gastric juice in patients with ulcer whether gastric, duodenal or at the stoma of a gastro-enterostomy The drug may decrease or completely relieve pain soon after it is given Methantheline (Banthine) bromide should be given parenterally or orally every 4 to 6 hours day and night in doses of 50 mg occasionally larger doses may be needed This schedule should be continued for 2 or 3 months a dosage decreased to 25 mg every 6 hours should then be maintained for a long time with a return to the greater dosage if symptoms recur or if some illness or psychic stresses occur in this sense the latter is a prophylactic procedure

Dryness of the mouth is usually troublesome in the first few days of treatment but tends to decrease later on Pupils will be dilated and this often hinders reading of fine print and will require the use of dark glasses in bright light or sunshine This being so methantheline (Banthine) bromide should not be used if the patient has glaucoma Some patients

yet in many instances it is simply evidence of lack of thoroughness in the treatment of the ulcer Very often it is caused by the patient s carelessness in not following his diet closely and in not taking antacids or by his falling back into old habits of drinking smoking and so on The term intractable should be reserved for cases that have had adequate supervised treatment which has failed to control the situation this usually *means obstruction or penetration*

Intractability of ulcer pain may represent an inadequate patient-physician relationship resulting in neurosis and dyspepsia Frequently on the other hand true intractability results from failure to neuralize the gastric acid adequately which will be shown if analyses of the gastric juices are being made When all measures of diet antacids and antispasmodics including methantheline (Banthine) bromide have failed to control pain in patients with recurrent ulcer attacks and in those apparently unable to maintain proper control deep roentgen therapy to the stomach may be tried This should be given by a skilled x ray therapist who decides both the dose (usually 165 roentgens daily until 1600 to 1700 roentgens have been given) and the technique to be employed If x ray therapy is unsatisfactory or a more permanent result is desired surgery should be advised The subtotal gastrectomy operation usually gives good results in this type of patient

Alkalosis may supervene in the alkali therapy of peptic ulcer When it occurs it generally does so (a) from the prolonged use of sodium bicarbonate or a preparation containing sodium bicarbonate (b) from the presence of impaired kidney function or (c) from obstruction and vomiting with loss of chloride Impaired renal function may have been evident but overlooked or it may have been incipient and not obvious on routine urinalysis The treatment of such alkalosis should consist in the withdrawal of the strong alkali and the substitution of a weaker acid neuralizing agent and forcing fluids Various forms of aluminum hydroxide gel or the newer colloidal preparations may be substituted for the Sippy type of alkali that has been used Under such circumstances it is well to withhold all antacid medication for several days to use an ulcer type of diet alone and to administer physiological saline solution parenterally 1000 to 2000 cc daily in addition to fluids by mouth Additional acid therapy is considered under Alkalosis After the alkalosis has been corrected proceed with an ulcer therapy in which milder antacids are used

Obstruction Pyloric obstruction associated with duodenal ulcer may

4 Hence, whenever you are exposed to any of the circumstances listed under 3, you should automatically take the following steps to prevent an ulcer recurrence
   a Be very sure to observe points 1 and
   b Take antacid 1 hour after meals and at bedtime
   c Go to bed earlier than usual You do not necessarily have to sleep but it is important for you to get extra rest in bed Rest on week ends Cancel social activities and all work that is nonessential
   d Observe this intensified form of treatment for at least 1 week As a rule it should be observed for as long as the aggravating factors listed under 3 are present

5 If you have any ulcer symptoms notify your doctor immediately

Other Measures In the past many types of measures have been introduced for the treatment of chronic duodenal ulcer, none of which has withstood the tests of time These have included such a variety as ochra bile, mucin and the once very enthusiastically prescribed histidine therapy None of these is recommended for use The reported results of the use of certain duodenal extracts and enterogastrone are too few at the present time to allow proper evaluation The most recent results are not too encouraging Corticotropin seems to be contraindicated

Complications

Certain complications from ulcer should be watched for closely and treated adequately Treatment for them however, should usually be conservative

Simple Bleeding Perhaps the most common complication is simple bleeding Thorough treatment of the ulcer as outlined in the preceding pages will usually cause the bleeding to stop The stools should be examined daily for occult blood to determine when bleeding has ceased Slow oozing of blood from the ulcer should be treated by careful observation and strict adherence to treatment schedule If bleeding continues and severe anemia develops iron liver, and transfusion may be necessary Usually rest and careful adherence to ulcer regime will give good results If bleeding becomes serious the patient should be treated for hemorrhage

Intractability of Ulcer Pain This might be considered a complication,

be due to muscular spasm edema scarring of tissue or a combination of these When it is due to spasm and/or edema, adequate medical treatment along with antispasmodics usually suffices In the case of unrelieved obstruction especially if there is cicatricial stenosis surgery is indicated For such obstructions the type of surgery to be used is still a matter for debate Many still prefer posterior gastro enterostomy, but the best permanent results are secured by subtotal gastrectomy Recently posterior gastro enterostomy combined with vagotomy has been advised Enthusiasm for vagotomy already seems to be waning If there is retention of gastric contents a tube should be inserted at periodic intervals and the stomach contents aspirated An antacid should then be given In patients who have night pain aspiration of gastric contents at bedtime will often give excellent relief of both pain and obstruction

Hemorrhage This refers to massive bleeding from an esophageal gastric, duodenal, or jejunal ulcer

Extensive hemorrhage from ulcer constitutes a medical emergency and demands confinement to bed preferably in a hospital Not infrequently, for reasons not well understood extensive bleeding has been going on for some time with little or no symptoms manifest until the patients vomits a copious amount of changed blood or passes a large tarry stool, followed by faintness weakness or even shock and collapse The clinical condition of the patient should receive first consideration with rest, avoidance of unnecessary examinations and the institution of conservative measures Statistically over 85 per cent of instances of massive hemorrhages from the gastro-intestinal tract are due to ulcer and for its treatment a cursory examination of the patient is usually sufficient to substantiate the diagnosis and to rule out other causes Extensive palpation of the abdomen should be avoided Morphine sulfate 8 mg should be given hypodermically for apprehension and restlessness Blood pressure should be taken only as necessary to evaluate the patient's status Too frequent determinations tire the patient and cause apprehension It is important to realize that transfusions are not always necessary They should be given however, when hematocrit readings fall below 25 per cent to debilitated aged and weakened patients and to those in shock Transfusions of whole blood or packed cells are necessary to replace red blood cells lost by hemorrhage If platelets are depressed fresh blood is recommended for the best results

be due to muscular spasm, edema, scarring of tissue or a combination of these When it is due to spasm and/or edema, adequate medical treatment along with antispasmodics usually suffices In the case of unrelieved obstruction especially if there is cicatricial stenosis, surgery is indicated For such obstructions the type of surgery to be used is still a matter for debate Many still prefer posterior gastro enterostomy, but the best permanent results are secured by subtotal gastrectomy Recently posterior gastro enterostomy combined with vagotomy has been advised Enthusiasm for vagotomy already seems to be waning If there is retention of gastric contents a tube should be inserted at periodic intervals and the stomach contents aspirated An antacid should then be given In patients who have night pain aspiration of gastric contents at bedtime will often give excellent relief of both pain and obstruction

Hemorrhage This refers to massive bleeding from an esophageal, gastric duodenal, or jejunal ulcer

Extensive hemorrhage from ulcer constitutes a medical emergency and demands confinement to bed preferably in a hospital Not infrequently, for reasons not well understood, extensive bleeding has been going on for some time with little or no symptoms manifest until the patients vomits a copious amount of changed blood or passes a large tarry stool followed by faintness, weakness, or even shock and collapse The clinical condition of the patient should receive first consideration with rest avoidance of unnecessary examinations, and the institution of conservative measures Statistically over 85 per cent of instances of massive hemorrhages from the gastro intestinal tract are due to ulcer, and for its treatment a cursory examination of the patient is usually sufficient to substantiate the diagnosis and to rule out other causes Extensive palpation of the abdomen should be avoided

Morphine sulfate, 8 mg should be given hypodermically for apprehension and restlessness Blood pressure should be taken only as necessary to evaluate the patient's status Too frequent determinations tire the patient and cause apprehension It is important to realize that transfusions are not always necessary They should be given however when hematocrit readings fall below 25 per cent, to debilitated aged, and weakened patients and to those in shock Transfusions of whole blood or packed cells are necessary to replace red blood cells lost by hemorrhage If platelets are depressed, fresh blood is recommended for the best results

be due to muscular spasm edema scarring of tissue, or a combination of these When it is due to spasm and/or edema adequate medical treatment along with antispasmodics usually suffices In the case of unrelieved obstruction especially if there is cicatricial stenosis surgery is indicated For such obstructions the type of surgery to be used is still a matter for debate Many still prefer posterior gastro-enterostomy, but the best permanent results are secured by subtotal gastrectomy Recently posterior gastro enterostomy combined with vagotomy has been advised Enthusiasm for vagotomy already seems to be waning If there is retention of gastric contents, a tube should be inserted at periodic intervals and the stomach contents aspirated An antacid should then be given In patients who have night pain aspiration of gastric contents at bedtime will often give excellent relief of both pain and obstruction

Hemorrhage This refers to massive bleeding from an esophageal gastric duodenal, or jejunal ulcer

Extensive hemorrhage from ulcer constitutes a medical emergency and demands confinement to bed preferably in a hospital Not infrequently for reasons not well understood, extensive bleeding has been going on for some time with little or no symptoms manifest until the patients vomits a copious amount of changed blood or passes a large tarry stool, followed by faintness weakness or even shock and collapse The clinical condition of the patient should receive first consideration, with rest, avoidance of unnecessary examinations and the institution of conservative measures Statistically, over 85 per cent of instances of massive hemorrhages from the gastro intestinal tract are due to ulcer and for its treatment a cursory examination of the patient is usually sufficient to substantiate the diagnosis and to rule out other causes Extensive palpation of the abdomen should be avoided Morphine sulfate 8 mg should be given hypodermically for apprehension and restlessness Blood pressure should be taken only as necessary to evaluate the patient s status Too frequent determinations tire the patient and cause apprehension It is important to realize that transfusions are not always necessary They should be given however when hematocrit readings fall below 25 per cent, to debilitated aged and weakened patients, and to those in shock Transfusions of whole blood or packed cells are necessary to replace red blood cells lost by hemorrhage If platelets are depressed, fresh blood is recommended for the best results

be due to muscular spasm edema scarring of tissue, or a combination of these When it is due to spasm and/or edema adequate medical treatment along with antispasmodics usually suffices In the case of unrelieved obstruction especially if there is cicatricial stenosis surgery is indicated For such obstructions the type of surgery to be used is still a matter for debate Many still prefer posterior gastro enterostomy, but the best permanent results are secured by subtotal gastrectomy Recently posterior gastro enterostomy combined with vagotomy has been advised Enthusiasm for vagotomy already seems to be waning If there is retention of gastric contents a tube should be inserted at periodic intervals and the stomach contents aspirated An antacid should then be given In patients who have night pain aspiration of gastric contents at bedtime will often give excellent relief of both pain and obstruction

Hemorrhage This refers to massive bleeding from an esophageal, gastric duodenal, or jejunal ulcer

Extensive hemorrhage from ulcer constitutes a medical emergency and demands confinement to bed preferably in a hospital Not infrequently for reasons not well understood, extensive bleeding has been going on for some time with little or no symptoms manifest until the patients vomits a copious amount of changed blood or passes a large tarry stool followed by faintness weakness or even shock and collapse The clinical condition of the patient should receive first consideration with rest, avoidance of unnecessary examinations and the institution of conservative measures Statistically over 85 per cent of instances of massive hemorrhages from the gastro-intestinal tract are due to ulcer, and for its treatment a cursory examination of the patient is usually sufficient to substantiate the diagnosis and to rule out other causes Extensive palpation of the abdomen should be avoided Morphine sulfate, 8 mg should be given hypodermically for apprehension and restlessness Blood pressure should be taken only as necessary to evaluate the patient's status Too frequent determinations tire the patient and cause apprehension It is important to realize that transfusions are not always necessary They should be given however when hematocrit readings fall below 25 per cent to debilitated aged and weakened patients and to those in shock Transfusions of whole blood or packed cells are necessary to replace red blood cells lost by hemorrhage If platelets are depressed, fresh blood is recommended for the best results

1 00 p m	Cream of vegetable soup (peas, carrots, potatoes, string beans asparagus), ground scraped or minced meat, fish boiled or mashed potatoes, vegetable purée (peas, carrots, asparagus) cooked strained fruit plain rice or tapioca pudding junket, jello, plain milk pudding chocolate cornstarch white bread and butter, tea
3 00 p m	Cocoa or tea
6 00 p m	Cream cheese or eggs (soft boiled or poached) boiled or mashed potatoes or cereal with milk and sugar
9 00 p m	Vegetable puree dessert from above list white bread and butter

In the experience of the authors the Meulengracht diet has not proved to be superior to the Sippy outline presented in the preceding pages, it is a fact that most patients for sometime after a hemorrhage refuse to take food including the Meulengracht diet, so its use is largely theoretical consideration and is not practical

Along with the preceding measures the patient should be started soon on iron in the form of ferrous sulfate or ferrous gluconate 0 3 to 0 6 gm 3 times a day Concentrated liver extract, 15 units (1 cc), may be given intramuscularly daily as adjuvant therapy Sedatives such as phenobarbital 15 mg , may be given 3 or 4 times a day and if necessary, antipasmodics may be used

By the third week, if the bleeding has stopped completely, and usually it has if the ulceration is non-malignant, the hemoglobin and red blood cell values should be rising, and the patient will have advanced in the dietary regime to 3 meals a day with interval feedings of milk, cream and antacids At this point if economic reasons demand it and the red blood cell count is still below 3,000 000 per cu mm , a transfusion may be given, although actually it speeds up recovery only temporarily Ordinarily the red cell count will have advanced to over 3 000,000 by this time and the patient may gradually begin to be out of bed Many believe that the patient if he is in the hospital should not be discharged until all evidences of bleeding have disappeared and

The initial treatment for hemorrhage from ulcer should be conservative since studies have shown that there is spontaneous cessation of bleeding in at least 70 per cent of these patients The patient should be kept warm and fluids to combat dehydration and electrolyte imbalance should be given parenterally slowly in the form of 5 per cent glucose or physiological saline or both

No attempt should be made to give any drugs by mouth to check the hemorrhage The Sippy method of treating hemorrhage is advised with adequate fluids administered parenterally and with careful observation of kidney function Give a powder of magnesium oxide 4 0 gm and calcium carbonate 2 0 gm at once and repeat this in half an hour For the next 8 to 10 hours give calcium carbonate 2 0 gm every half hour In the following 24 hours 2 0 gm of calcium carbonate should be given every half hour through the day and every hour through the night On the third day it is time to begin the progressive Sippy diet of hourly feedings of milk and cream with alkalis on the half hours between the milk and cream feedings

The Meulengracht regime for the treatment of hemorrhage from ulcer is based on the principle of quite full feeding from the start using a high calorie puree diet adequate in proteins to aid the body in replacing hemoglobin that has been lost It includes further the use of alkalis antispasmodics and iron The alkali should consist of 1 teaspoonful equal parts of sodium bicarbonate and magnesium subcarbonate with a small amount of the tincture of hyoscyamus 15 drops 3 times a day The Meulengracht diet follows

MEULENGRACHT DIET FOR BLEEDING PEPTIC ULCER

First Day	6 00 a m	White bread and butter tea
	9 00 a m	Oatmeal with milk white bread and butter
	1 00 p m	Vegetable puree (peas carrots) mashed potato white bread and butter tea
	3 00 p m	Cocoa or tea
	6 00 p m	Mashed potato vegetable puree custard white bread and butter tea
Second Day and Thereafter	6 00 a m	White bread and butter tea
	9 00 a m.	Oatmeal with milk white bread and butter

48 hours after the bleeding seems to have stopped, if the clinical condition of the patient is fairly good

Perforation Acute perforation of a gastric, duodenal, or jejunal ulcer, of which duodenal is by far more common, is the principal cause of death in ulcer disease and so demands immediate surgical treatment with closure of the perforation Every hour of delay causes a sharp rise in the mortality rate Perforation may complicate massive hemorrhage Pre-operative preparation of the patient must be carried out as expeditiously as possible with transfusion of blood for shock being given while the operation is in progress Simple closure of the stoma is advised

Since the peritoneum has been contaminated by gastro intestinal contents antibiotic therapy by systemic administration is advised Aureomycin 0 5 to 1 0 gm by mouth 4 times a day (or 0 5 gm in 250 cc saline intravenously every 12 hours with an aqueous suspension of procaine penicillin 300 000 units intramuscularly 2 times a day, is excellent Chloramphenicol 0 5 to 1 0 gm orally or intravenously 4 times a day, is also excellent in combatting the mixture of organisms present Strep mycin 1 0 to 2 0 gm intramuscularly in combination with penicillin aureomycin, or chloramphenicol makes a highly effective treatment, apparently there is not the same antagonism between streptomycin and other antibiotics as exists in the case of penicillin Fluid and electrolytic balance should be maintained with 5 per cent glucose and/or physiological saline solution

Surgery for Gastric Ulcer

The vast majority of patients with ulcer — over 85 per cent — respond favorably to careful medical management Therefore surgical treatment for ulcer disease should be restricted to certain complications For simple ulceration in the lower third of the esophagus surgery is seldom required In the case of gastric ulcer when there is any reasonable doubt of its non neoplastic nature partial or subtotal possibly total resection should be carried out For perforation of either a gastric or a duodenal ulcer immediate operation is indicated For actual cicatricial stenosis of the lower end of the esophagus or of the pylorus surgery is advisable In patients who have a chronic recurring duodenal or gastric ulcer and who cannot or will not, follow a strict ulcer regime subtotal gastrectomy is also advisable

the red blood count is over 4 000 000 cells Actually however home treatment is now just as satisfactory as hospital management

Occasionally the question of surgical intervention for bleeding ulcer becomes a problem of considerable magnitude It is claimed that for an individual past the age of 50 particularly with advanced arteriosclerosis in whom evidence of continued bleeding is of more than slight degree surgery limited usually to thoroughgoing ligation of the bleeding vessel should be carried out However the evidence for this is not great and surgery for bleeding of this type is increasingly being given up With active bleeding vagotomy is especially contraindicated some have advocated vagotomy however for cases of recurrent bleeding carried out after careful medical treatment of the hemorrhage This is of dubious value and cannot be recommended Extensive surgery in such patients is seldom well tolerated Continued bleeding is very often due to neoplastic rather than to peptic ulceration This must be kept in mind and every effort made to recognize the early cancer so that it can be operated on at once with hope for complete removal

In order to set up quantitative criteria some have stated that any patient in whom an arbitrary amount of 1500 cc of blood replacement is required daily to maintain equilibrium should have operative intervention This has been called the test of transfusion Others feel that if bleeding is still continuing after the administration of 2500 cc of blood surgery should be performed at once This group of patients as previously mentioned will nearly all be over 50 years of age and will be comparatively small The question of surgery should not be debated too long lest the condition of the patient become rapidly worse and result in a fatal operation When surgical measures are performed as a last resort after repeated episodes of bleeding the mortality is high Satisfactory criteria of when to operate and when not to in this group of patients are still lacking

Another question that arises frequently particularly in the patient not already known to have an ulcer is when to perform x ray studies in the patient who has just had a gastro-intestinal hemorrhage If delayed for several weeks blood clot in the ulcer may obscure the niche or the ulcer may have healed and no source of bleeding be found More and more early x ray examination is being practiced since it has been learned that when done carefully without manipulation (kneading) of the abdomen the procedure carries little risk of harm even when done in the first few days following the bleeding even within

ulcer Vagotomy is being used less and less because of the increasing number of patients in whom results are not too satisfactory

Certain post-vagotomy symptoms may occur that require treatment The presence of pain may signify the persistence of an ulcer or ulcer ative recurrence to be managed by medical treatment as outlined in previous pages Bleeding and perforation may occur after vagotomy and should be treated as already discussed The abdominal fullness nausea, and eructations may be helped by increasing gastro intestinal tone with the administration of urethane of beta methylcholine chloride (Urecholine) subcutaneously intramuscularly, or by mouth The par enteral dose produces the most prompt action, the effects by oral route are less intense The dose by subcutaneous or intramuscular injection should be 5 mg either before meals or 2 hours after meals This amount may be repeated as often as every 4 hours The oral dose is 5 to 10 mg, best given on an empty stomach to avoid nausea The drug should not be used after recent intestinal anastomosis, in the presence of vesical (bladder) neck obstruction, or in patients with hyperthyroidism, asthma coronary sclerosis, known heart disease or pregnancy Urecholine should be used cautiously in elderly patients Diarrhea can usually be controlled by the administration of an antispasmodic such as atropine sulfate 0 6 mg, and possibly a sedative such as phenobarbital 15 mg several times a day for a week or two Either bismuth or kaolin may be given as adjuvant therapy

Duodenitis

Frequently this accompanies an ulcer of the duodenum Its manage ment is part of the therapy of Duodenal Ulcer Also duodenitis may be an accompaniment of gastritis or be independent of that Its treatment should be that described for Gastritis

Duodenal Diverticulum and Diverticulitis

A diverticulum needs no treatment unless it bleeds or perforates, then the treatment is that described for these complications of Ulcer Diverticulitis should be treated by withholding diet and by other meas ures advised for Appendicitis including possible surgical exploration and excision

Gastro enterostomy Gostro enterostomy either anterior or posterior as a single procedure for either gastric or duodenal ulcer has been almost entirely abandoned

Subtotal Resection of the Stomach Subtotal resection of the stomach seems to have become the operation of choice for a gastric ulcer causing symptoms not responding to medical measures possibly for those with frequent recurrence of hemorrhage and for those that fail to heal completely under a strict medical regime and are consequently suspected of being cancerous In the opinion of many physicians it is the operation of choice when surgery is indicated in the treatment of a duodenal ulcer Bloating nausea and the dumping syndrome are rather common symptoms after subtotal resection of the stomach and a complicating jejunal (marginal) ulcer occurs in between 3 and 10 per cent of cases In almost all of these patients digestion is far from normal and weight loss and much post prandial discomfort are the rule The probability of these must be kept in mind while the physician is deciding for or against subtotal resection of the stomach

Vagus Resection Resection of the vagus nerves to the stomach vagotomy in the treatment of duodenal or marginal ulcer is based on the physiological principle that interruption of the vagus nerve supply to the stomach decreases the neurological stimulus of gastric acid formation Also motor function of the stomach is decreased by vagotomy This operation at first performed only on intractable cases then widened in scope is narrowing again to instances of (1) marginal ulceration (2) intractable pain with presumably a strong emotional phase of gastric secretion unrelieved by strict medical management and possibly (3) instances of recurrent hemorrhage The first approach was transthoracic but that is largely being replaced by a transabdominal route combined with posterior gastro enterostomy and/or pyloroplasty The latter addition to the procedure has aided considerably in relieving the gastric distention so commonly present after operation The major advantage to the abdominal approach for vagotomy is that the ulcerated area can be examined and simultaneous gastric resection or gastro-enterostomy performed if necessary Vagotomy should not be performed in the presence of pyloric obstruction unless a gastro enterostmy or pyloroplasty is done at the same time The contraindications to vagus resection include active bleeding at any age at the time of operation recent massive hemorrhage in patients over 50 years of age and any diagnostic uncertainties about the presence or absence of duodenal

seldom is high so antacids need not be an important part of therapy If the condition is marked with severe pain, or with such complications as hematemesis or obstruction, surgical exploration may be indicated Some advise opening the stomach to reduce the redundant mucosa, with simple resection and closure, or resection of prolapsed mucosa with pyloroplasty, or gastric resection, or finally, gastroenterostomy With either medical or surgical treatment, relief of symptoms may not be complete

BIBLIOGRAPHY

1 BERK, J E "Recent Advances in Drug Therapy of Peptic Ulcer," *Am Jour Med Sc*, 1951, CCXXI p 567
2 DRAGSTEDT L R 'Appraisal of Vagotomy for Peptic Ulcer after 7 Years *Jour Amer Med Assoc*, 1951, CXLV, p 795
3 GLENN F 'Present Status of Surgical Treatment of Peptic Ulcer' *Jour Amer Med Assoc*, 1951, CXLV, p 790
4 GRAY, S J and McCOMBS R P "Peptic Ulcer Therapeutic Conference *Bull N E Med Center*, 1950, XII, p 80
5 HEALY, M J Jr HELLMAN S J, and SAVER P K 'Vagotomy Versus Gastric Resection" *Jour Amer Med Assoc*, 1951, CXLVII, p 368
6 KIRSNER, J B PALMER W L, LEVIN, E, and KLOTZ A P 'Gastric Antacid and Anti Secretory Drugs A Survey Based Primarily on Their Effects upon Gastric Secretion in Man' *Ann Int Med*, 1951 XXXV p 785
7 LYONS R H and BRENNER, C Erythropoiesis following Bleeding Peptic Ulcer, *Am Jour Med Sc*, 1939, CXCVIII p 492
8 PALMER, W L KIRSNER, J B and LEVIN, E "An Internist Views the Surgical Treatment of Peptic Ulcer' *Jour Amer Med Assoc*, 1951, CXLV p 1041
9 PALMER, W L, KIRSNER J B, and LEVIN, E. The Treatment of Intractable Peptic Ulcer *Ann Int Med*, 1950 XXXIII p 590
10 SCHNITKER, M A, and EVANS, W A Jr 'Peptic Ulcer A Study of the Disease before and after the Demonstrated Ulcer" *N E J Med*, 1936 CCXIV p 198
11 WALTER, W and BELDING, H H III 'Clinical Studies on 130 Patients One to Four Years after Vagotomy," *Proc Staff Meet Mayo Clinic*, 1951 XXVI p 199

Dilatation Chronic Duodenal Ileus

This may be relieved by the patient s lying face down with the foot of the bed elevated 10 to 12 inches by his lying on the left side with the foot of the bed similarly elevated or by his taking the knee chest posi tion It may be part of visceroptosis and largely of neurotic origin man agement for visceroptosis will be appropriate and should be tried Duodenal ileus may be acute with or without accompanying acute dilatation of the stomach If the latter is present tube drainage of both is advised for these patients Any accompanying constipation should be treated If it is not relieved or if it becomes recurrent and is repeatedly very annoying with probable adhesions or drag at its point of fixation at the duodeno ileal juncture surgical intervention should be discussed with a surgeon skilled in surgery of the gastro intestinal tract

Neoplasms

Carcinoma of the duodenum is rare if it occurs its treatment should be surgical Polyps are a little more frequent and may be the site of bleeding or may cause obstruction Surgical treatment may be needed *if there is obstruction not relieved by tube drainage or recurring ob* struction surgery will often be imperative What has been stated about polyps applies also to benign neoplasms of the duodenum

Prolapse of Gastric Mucosa into Duodenum

There is no doubt that varying degrees of prolapse of gastric musoca into the duodenum occur but considerable controversy exists concern *ing the clinical symptoms it produces if any and how it should be* treated Both gastritis and duodenal ulcer seem to be associated fre quently and may be the cause of symptoms more than the prolapse itself In fact the symptoms that have been described for prolapse may simulate closely those of duodenal ulcer duodenitis gastritis and neoplasm If *gastric prolapse is demonstrated by roentgen ray or by operation and it is thought to be causing symptoms the treatment recommended is* medical with a bland diet antispasmodics such as atropine oxyphe nonium (Antrenyl) bromide and propantheline (Probanthine) bromide to lessen peristaltic activity With mucosal prolapse gastric acidity

12 WARTHIN T A WARREN R and WISSONG E G Combined Medical and Surgical Management of Upper Gastro-intestinal Hemorrhage *N E J Med* 1949 ccxli p 473
13 RAPPAPORT E M RAPPAPORT E O and ALPER A Incidence and Clinical Significance of Transpyloric Prolapse of Gastric Mucosa *Jour Amer Med Assoc* 1952 cl 182
14 FELDMAN M MORRISON S and MYERS P The Clinical Evaluation of Prolapse of the Gastric Mucosa into the Duodenum *Gastroent* 1952 xxii 80

saline solution, repeated as needed to counteract the dehydration, should be given

With much rectal irritation causing uncomfortable tenesmus, the installation of 60 cc of a starch enema containing 20 drops of tincture of opium every 6 hours often gives much comfort and stops repeated small bowel movements if they are taking place

After 24 hours a low-residue diet should be started with frequent feedings at first For this, various broths of beef, mutton, or chicken, crisp toast, tea or coffee, gelatin and cooked eggs along with water should be given every 2 hours If this goes well and the diarrhea ceases potato pureed vegetables custards simple puddings, and stewed fruits should be added As a rule an ordinary diet can be resumed in 1 week Milk even if boiled is inadvisable in the first week, as it leaves a large residue Some physicians, however, do give boiled milk early in the disease and claim excellent results

As to the use of various drugs such as aluminum hydroxide (Amphogel) kaolin and pectin (Kaopectate) aluminum hydroxide and kaolin (Kaomagma), bismuth subgallate tannin proteinate, acetyltannic acid kaolin et cetera there is much difference of opinion among excellent practitioners These powders however, are generally used in repeated tablespoonful doses with good results claimed for them in restoring bowel movements to normality and probably in making multiplication of the causative bacteria in the intestinal tract more difficult

When the diarrhea is over, most patients are disturbed because they are having no stools or only very small ones and wish to take a cathartic They should be told that it is normal after diarrhea has emptied the bowel and the diet has been one of small residue to have slow return to movements of normal frequency and bulk, and they should be advised to refrain from taking cathartics An enema of warm normal saline solution each morning may facilitate return to normality of bowel movements

Chronic Diarrhea Of first importance is to find the cause of any continuing or often repeated diarrhea even if it is slight in amount If no cause is discovered the following plan of treatment should be followed A period of several weeks of bed rest is advisable If bowel movements are very frequent complete bed rest with use of bedpan and urinal should be enforced if bowel movements are not very frequent toilet privileges may be allowed and a tub bath permitted once a day Obviously these patients should be spared from worry as much

CHAPTER XL

DISEASES OF THE INTESTINE

Diarrhea in General Non specific Diarrhea

By these terms is meant a diarrhea not caused by a demonstrated causative parasite or bacterium or by a food poison The treatment of these has been described on earlier pages under these several organisms or diseases *for example bacillary dysentery* intestinal tuberculosis cholera food poisoning amebiasis ulcerative colitis hyperthyroidism et cetera Often much of the treatment described here is applicable to diarrhea incident to these other conditions

Acute Diarrhea The patient should be kept in bed and no food allowed for 24 hours cracked ice may be sucked and a small amount of water given If there is vomiting the stomach should be washed out *with a weak solution of sodium bicarbonate The former practice of* cleaning out the intestinal tract with castor oil has been abandoned very generally because it does not seem that an intestinal tract emptying itself by an active diarrhea would be benefited by more bowel movements produced with a drug

On the contrary it seems advisable to check watery bowel movements soon and to this end camphorated tincture of opium [paregoric] *should be given in doses of 1 or 2 teaspoonfuls repeated after* each watery movement If there is much tenesmus and moderate abdominal cramps it is especially helpful When these symptoms are very marked some advise giving a hypodermic injection of 15 mg of morphine sulfate with 0 5 mg of atropine sulfate

Many of these patients are chilled sweating and in moderate vasomotor collapse For them blankets and hot water bottles should be used *the latter with great caution to prevent skin burns If the collapse* is marked treatment for shock should be used With diarrhea continued beyond 24 hours there may be considerable dehydration if these patients are unable to take water by mouth an infusion of 500 cc of normal

Fruit	None	All
Meat egg or cheese	Tender beef lamb fowl (not fried) fresh or canned fish cheese eggs except fried	Tough stringy meat
Potato or substitutes	Baked boiled or creamed potatoes macaroni spaghetti noodles rice (except wild rice)	Unrefined (wild) rice
Soups	Broths bouillon strained cream soups	Vegetable soup
Sweets	Sugar syrups honey (strained) jelly plain candies	Jams candies containing fruit or nuts
Vegetables	None (see footnotes)	All (see footnotes)
Miscellaneous	Cream sauces gravies peanut butter vinegar spices in moderation	Nuts pickles olives relishes popcorn

Additions from following list but not more than 1 item per day

1 Ripe banana or orange juice
2 Tomato or other vegetable juice
3 Boiled milk fresh pasteurized milk non fat milk solids cream as tolerated
4 Cooked or canned apples avocado apricots peaches pears prunes all without skins or seeds
5 Cooked or canned asparagus pureed vegetables except corn

In the diet it is important to include vitamins in amounts not less than that specified after each item vitamin A 5,000 international units thiamine 3 mg riboflavin 4 mg niacinamide 20 mg, ascorbic acid 100 mg

Largely as a diagnostic measure when stool examination has failed to demonstrate amebae or their cysts it is advisable to give an antibiotic, as described under Amebiasis or 60 mg of emetine, hypodermically twice daily for 3 days If diarrhea ceases presumably amebiasis is the cause and the patient should then be treated thoroughly for this disease

Much effort to treat these patients by change of intestinal flora has been applied but with very questionable results Usually cultures of *Lactobacillus acidophilus* along with feeding lactose have been utilized The results obtained scarcely justify the procedure

Sometimes diarrhea usually fairly moderate may be a form of carbohydrate indigestion and can be managed by reducing the carbohydrate moiety of the diet particularly by omission or reduction of starchy foods potatoes in particular A rare diarrhea is caused by absence of

as possible The help of a wise psychiatrist is often needed since not infrequently a non specific diarrhea is more psychic than somatic in origin For the restless patient moderate sedation will often help much in the management of his diarrhea

Colonic irrigations are not to be given usually certainly not routinely In some patients however a cleansing enema of warm normal saline solution particularly just before time for the patient to begin the night s sleep will be soothing and result in a considerable period of freedom from bowel movements

Drugs of a kind presumed to decrease intestinal peristalsis are usually disappointing in their results with chronic diarrhea as well as with acute However any of the drugs may be tried but should not be persisted in when they do not seem to benefit They have been enumerated under Acute Diarrhea Possibly calcium is an exception in this category the patient may be tried with 1 gm tablets of calcium 1 to 3 such tablets being chewed and swallowed 3 hours after each meal or with 1 heaping teaspoonful of basic calcium phosphate dissolved in half a glass of hot water and then allowed to cool drunk 3 hours after meals Anti spasmodic drugs such as tincture of belladonna usually prove ineffective Sulfonamides and antibiotics should be tried as discussed under Chronic Ulcerative Colitis

These patients should be given a low residue diet made up from the following list of suggested food items which will cause a minimum of irritation to the mucous membrane of the intestinal tract

ITEMS FOR LOW RESIDUE DIET

	Foods included	*Foods excluded*
Beverages	Tea postum or other cereal beverage coffee decaffeined coffee carbonated beverages (cooled but not iced) milk or thin cream and sugar in tea and coffee	Milk
Breads	Enriched white bread fresh or toasted white crackers	Whole grain cereals and rye bread
Cereals	Refined cereals made from wheat corn or rice strained oatmeal	Whole grain cereals
Desserts	Custard pudding gelatin and rennet desserts ice cream plain cake and cookies	Desserts containing fruit or nuts

should be maintained, if necessary, parenterally. Usually ascorbic acid 100 mg, thiamine 10 mg, and niacinamide, 20 mg, should be given in the infusion solution for the first day or two and then they may be given by mouth.

Sulfonamides and antibiotics, as discussed under Ulcerative Colitis and Bacillary Dysentery, should be used unless the diarrhea ends quickly.

As the diarrhea lessens, it is often helpful to give a mixture of aluminum hydroxide and kaolin (Kaomagma), 4 to 8 cc. in milk, until the stool shows discoloration from the drug. Carob flour (Arobon), a palatable, high-pectin containing substance is useful in these cases. Children should be given 1 level tablespoonful in 120 cc. of milk every 2 to 3 hours, and infants 2 teaspoonfuls in 120 cc. of skimmed milk or water. The liquid should be boiled for ½ minute to sterilize it before it is given to infants and young children. The preparation contains some nourishment, is palatable, and has a strong antidiarrheal action.

If peristalsis is excessive, colic violent, and movements very frequent and watery, the camphorated tincture of opium [paregoric], depending on the age of the child, 0.3 to 0.6 cc. every 4 hours, should be given by mouth, or if prompt action seems needed, morphine sulfate 0.3 to 1.3 mg., with atropine sulfate 0.065 to 0.25 mg., should be given hypodermically.

During convalescence, especially if warm weather continues, children who have had diarrhea should be watched carefully and kept on a restricted diet, but one completely adequate in calories and content. Cathartics probably should never be given to these convalescent children; constipation, if actual, calls for the use of non-irritating enemas.

Appendicitis

Whenever there is the possibility of acute appendicitis, give no cathartic, since cathartics by increasing peristalsis are apt to spread any peritoneal infection and lead to extensive, probably general, peritonitis. Also give no form of opium or similar sedative so long as a positive diagnosis has not been made, since by doing so important symptoms, especially localized pain, may be masked, increasing the difficulty of recognizing appendicitis. Early surgical consultation is imperative; the surgeon should take over management of the patient and decide whether to operate and if so when. If there must be any delay in the surgeon's visit, the physician will do well to give procaine penicillin in aqueous

free hydrochloric acid from the stomach and can be cured by giving 2 to 10 cc of dilute hydrochloric acid after meals the exact amount needed being determined by trial

Diarrheal Disease in Children Diarrhea in children naturally needs some variations from the treatment recommended for adults Dehydration is a usual result of diarrhea in children and should be kept in mind so that if insufficient water is being taken by mouth normal saline solution can be given subcutaneously 15 cc per pound weight of the child and repeated as needed to correct the dehydration when there is early mild dehydration

For infants and children with severe dehydration and electrolyte imbalance replacement therapy should be carefully carried out After determining the chemical status by finding hematocrit carbon dioxide chloride potassium and sodium values 20 cc per kilogram of body weight of a solution containing 3 volumes of 5 per cent glucose 2 volumes of isotonic saline and 1 volume of isotonic 1/6 molar sodium lactate is given promptly This is usually administered in a period of 1 hour and then an additional 20 to 40 cc per kilogram is given slowly In addition 5 per cent glucose 150 cc per kilogram of body weight is also given during the first 24 hours

If there is a deficiency in potassium as there usually is in severe cases a mixture of 1 0 gm of potassium chloride 0 5 gm of sodium chloride and o cc of 1 molar sodium lactate made up to a volume of 300 cc with distilled water is given subcutaneously in a dose of 50 cc per kilogram of body weight

If anemia is present transfusions of blood 20 cc per kilogram of body weight should be given In the presence of a state of shock blood or plasma in this dosage is very useful and should supplement other forms of therapy

If the stools are alkaline carbohydrates should dominate in the diet if acid beef juice and egg albumen should dominate If the child is being given milk skimmed milk is preferable for a time to whole milk Buttermilk is often well tolerated Various proprietary foods including diluted condensed milk may be well taken Food and fluids by mouth should not be withheld Protein should be given early and amigen solution 5 per cent and dextrose 5 per cent can be given as a portion of the glucose solution when there is a protein lack Care must be taken to maintain the proper number of calories however and consequently glucose intake must be kept adequate to cover this need Vitamin intake

Chronic Ulcerative Colitis

At the present time the most important features of treatment of chronic ulcerative colitis of any etiology, generally agreed upon are (1) prolonged rest, usually bed rest, with protection from worries of all sorts, and (2) as soon as is possible in relation to diarrhea, a low residue diet high in calories with protein content as great as 100 or even more grams and rich in vitamins Usually purified vitamins supplementary to those contained in the foods selected for the diet are given If a definite etiology can be established, treatment with appropriate drugs antagonistic to the causative organism should be utilized as described elsewhere in this volume under headings indicating the organism such as Amebiasis Bacillary Dysentery et cetera However in many patients with ulcerative colitis the causative mechanism is unknown

Rest flat in bed for a long period of time is essential for almost all of these patients certainly for as long as fever continues and usually well beyond its cessation Then return to ambulant life should be by a very gradual progression Ulcerative colitis is a very debilitating disease, and often these patients become emaciated, practically all lose considerable weight and adipose tissue largely disappears from beneath the skin This necessitates great care to prevent decubitus all the more so because the diarrheic patient is prone to get soiled from lack of bowel control and difficulty in thorough cleansing and drying after bowel movements Pressure from the bedpan increases this danger, a really comfortable easily managed bedpan is still to be invented A well trained, competent nurse and a comfortable hospital type of bed, one that can be moved about easily and one in which supine to semi reclining position for the patient is possible are necessities for proper care With the attendant fever sweating is frequent, which increases the need for frequent sponging drying and powdering of the back

Securing relaxation and freedom from worry and care for the patient is a very important part of rest therapy Permitting the patient to relax from strict adherence to the therapeutic program, including bed rest will often help in the struggle against the depression incident to a disease like chronic ulcerative colitis the gain in morale and appetite will more than offset the possible harm from relaxing the theoretically necessary restrictions

This is a type of patient who has always been of the worrying, apprehensive neurotic type and in whom the attack of ulcerative colitis has

suspension intramuscularly in a dose of 300 000 units and repeat in 6 hours if necessary Some prefer aureomycin or terramycin by mouth in a 2 gm dose daily but the nausea and vomiting so often present may contraindicate their use The surgeon may recommend treatment by posture with patient immobile in bed suction drainage by means of a tube passed through the stomach into the intestine and the use of opium with delayed instead of immediate appendectomy

With chronic appendicitis prompt appendectomy should not be the rule There will be ample time to use available diagnostic procedures Then when the diagnosis seems reasonably certain an interval appendectomy should be carried out Repeated consultations between physician and surgeon are desirable since without them an unnecessary appendectomy ensues leaving the patient unrelieved of his complaints or often with even more than existed before operation

Regional Ileitis Cicatrizing Enterocolitis Regional Segmental Colitis

Treatment of this whether medical or surgical in general remains unsatisfactory Obstruction or perforation when they occur necessitate prompt surgical treatment Surgical excision of involved parts of the bowel is rarely curative unfortunately since return and extension of the process is the usual sequence although this may be delayed Consequently excision of involved loops of intestine should not be advised until palliative treatment has failed and symptoms of partial obstruction have become very disturbing For palliation the patient should be put on a diet low in residue as described for Ulcerative Colitis and diarrhea if present should be treated as described for Ulcerative Colitis For moderate anemia ferrous gluconate should be used in dosage of 0 3 to 0 6 gm 3 times a day For more marked anemia transfusions of 300 to 500 cc should be used Corticotropin 50 to 100 mg intramuscularly daily or cortisone 100 to 150 mg intramuscularly or by mouth daily are helpful in giving temporary relief Through their use an obstruction may be relieved sufficiently to avoid surgery temporarily

Constricting Endometriosis

Excision of the lesion is rarely necessary X-ray or surgical sterilization should be done since these procedures are usually curative

The seriously ill patient who cannot tolerate food by mouth without serious exacerbation of diarrhea should have the gastro intestinal tract placed at nearly complete rest for 10 days to 2 weeks by the use of parenteral therapy Protein hydrolysate given intravenously as a 5 per cent solution dissolved in 5 per cent glucose is excellent Usually 1500 to 2000 cc are given daily Patients receiving protein hydrolysate must first be tested for any allergic reaction to the preparation since serious anaphylactic reactions can occur Unfortunately veins tend to thrombose nausea and vomiting may appear, and occasionally chills and pyrogenic reactions complicate parenteral medication

Supplementary vitamin therapy especially with vitamins of the B complex, is recommended since through diarrhea, poor diet, and improper absorption of food deficiencies of these vitamins and especially of thiamine hydrochloride are usually present Occasionally deficiencies of vitamins A C, and K also develop In seriously ill patients on parenteral therapy, purified vitamins may be added to the infusion fluid or be given by intramuscular injection For most patients the supplementary dose should be from 5 to 10 times the normal daily requirement If there are indications of a lack of any particular vitamin, additional amounts of the vitamin should be given as described under Vitamin Deficiencies

Ulceration and the loss of electrolytes, fluid protein and blood, which occurs in varying degrees depending upon the severity of the diarrhea, must be corrected promptly Parenteral physiological salt solution 1 or 2 liters daily, is recommended if dehydration is not extreme In hot weather or when there is severe dehydration parenteral fluid should be increased to 3 or even 4 liters of physiological salt solution If there is acidosis at least 1 liter, and if indicated 2 liters, of the parenteral solution should contain 5 per cent glucose If there are signs of potassium deficiency, at least 1 liter of a solution containing dibasic potassium phosphate 2 0 gm monobasic potassium phosphate 0 4 gm and glucose 50 gm should be given intravenously, the dose should be repeated if there is still a lack of potassium Patients showing a deficit in potassium should be given food by mouth as soon as possible

Calcium deficiency may also appear and when present is readily corrected by the administration of 10 cc of a 10 per cent solution of calcium gluconate intravenously, repeated as needed Calcium gluconate may be added to an infusion of physiological saline if desired

often followed some psychic upset or emotional trauma In this sense it is a psychosomatic disease needing both psychic and somatic therapy Often the aid of a wise psychiatrist will help by uncovering and controlling psychic situations not obvious on the surface but actually very disturbing The psychiatric approach will be a valuable adjutant to somatic therapy for patients with ulcerative colitis but psychoanalysis more often than otherwise has failed to help and sometimes it has aggravated the patient s diarrhea and other symptoms

Patients with lesions confined to the lower bowel and with slight or only very moderate diarrhea do not need complete bed rest beyond a few days for thorough study and evaluation of the situation These patients may even be treated with nothing more for rest than an afternoon nap and 10 hours in bed at night Between this group and the severely ill patient there will be all gradations with wide variation between prolonged complete bed rest and bed rest punctuated by different amounts of out of bed activity the physician determining all of this on the basis of the activity of the patient s disease

Diet In the acute phase with excessive diarrhea and not infrequently nausea all feeding except of water should be stopped for a day or two and if water can be taken only in small amount and dehydration develops parenteral normal saline solution with 5 per cent glucose should be given in amount to correct dehydration Then frequent feedings of beef, mutton or chicken broths flavored gelatins and soft boiled eggs should begin with gradual additions of various non residue foods such as potatoes custards simple puddings and tea or coffee with sugar and cream as the patient s condition betters Some of these patients will tolerate boiled milk and that can be given

As the general condition continues to improve and fever lessens various food items listed in Table vi on page 407 should be added to increase the protein intake and total calories gradually with supplemental vitamin intake of 5 to 10 times the normal requirements More often than not the physician errs in treating chronic ulcerative colitis by giving a diet that is too limited particularly one too low in protein content

Very often skilled nursing care means the difference between the patient s getting a too meager food intake and an adequate one Most of these patients are very weak and need to be fed being coaxed or even wheedled to eat more this takes time especially when the patient besides being weak physically is slowed mentally and is consequently inattentive A good nurse is essential to the proper diet regime

Camphorated tincture of opium [paregoric] and codeine are often useful when there is considerable pain and tenesmus At times drugs such as aluminum hydroxide gel bismuth subgallate, tribasic calcium phosphate kaolin aluminum hydroxide with kaolin (Kaomagma) and kaolin with pectin (Kaopectate) should be tried in doses of 30 to 60 cc a day Carob flour (Arobon) . tablespoonfuls in 1.0 cc of milk or water every 2 to 3 hours may also be useful in some patients

The rule that should be followed in the use of any of these drugs is to give them for a trial week and then continue or discontinue their use depending on whether they have seemed beneficial as judged by frequency of stools and the general condition including the fever of the patient

Surgery There are two schools of thought regarding surgical treatment of chronic ulcerative colitis One advises ileostomy when other methods of treatment have not been satisfactorily effective With the improved results now being obtained through medical treatment as described in the preceding pages surgery is being used with decreasing frequency by this group The other group recommends surgery only when complications develop such as stricture polyps fistula, or protracted vomiting In these cases for a time at least surgery is elective On the other hand if actual obstruction rectal abscess or perforation occurs immediate surgical treatment is imperative

If ileostomy has been done and results have been satisfactory then consideration should be given to the desirability of restoring the continuity of the gut by closing the ileostomy If this is done there is the possibility of the lesions of ulcerative colitis returning and this possibility should enter into the consideration of further surgery In some patients especially those in whom ulcerative lesions persist distal to the site of the ileostomy and continue to drain purulent material which is discharged through the rectum or bleed periodically, or in case polyposis develops colectomy is advisable In some patients mere difficulty in managing bowel movements through the ileostomy opening with incident discomfiture makes colectomy advisable If malignancy develops especially in a polyp colectomy with removal of the neoplasm becomes imperative

These various indications for possible or imperative surgery are very important in the therapy of ulcerative colitis Consequently early and repeated consultation with a wise surgeon skilled in gastro intestinal surgery is most desirable

Blood transfusion should be given *when there is severe blood loss* This measure is most helpful and should not be long withheld In fact even if anemia is not severe a daily transfusion of 50 to 500 cc of *carefully matched whole blood given for 3 to 5 days can be very helpful* in lessening diarrhea in reducing fever and in promoting a better feeling of *well being in these cases* Patients with low serum proteins are greatly benefited by infusions of plasma and especially albumin when the latter is available

Colonic Irrigations and Fecal Antiseptics Disinfectant colonic irrigations of any sort are not advised their use has seemed harmful rather than beneficial and they will not bring about any effective disinfection of the colon in these patients At times but not often gentle irrigation with warm normal saline solution will be beneficial This applies particularly to their soothing cleansing effect if given in small amount just before the patient goes to sleep at night since they may be followed by a period of freedom from bowel movements and tenesmus and allow the patient more prolonged restful sleep They should be used in this way if trial indicates such effect

Drugs The use of sulfonamides and antibiotics in patients with chronic ulcerative colitis has proved disappointing A trial of them is worth while however if care is taken that they cause no toxic reactions Sulfadiazine phthlalylsulfathiazole (Sulfathalidine) sulfisoxazol (Gantrisin) and sulfadimetine (Elkosin) have seemed to competent students of the subject to be the ones likely to be effective in sufficient degree to justify their use while at the same time they are less likely to cause toxic reactions They should be given in divided doses totaling 4 to 8 gm per day In an occasional patient severely ill with high fever penicillin in doses of 50 000 units every 3 hours has been effective and a trial of it is advised Other antibiotics including streptomycin aureomycin and terramycin have not seemed useful Corticotropin and cortisone may have a useful action in the acute phase but in most instances benefit is temporary Therapy must be prolonged over a period of 4 to 8 weeks and there is a risk of increasing or initiating intestinal bleeding A dose of corticotropin 25 to 50 mg or cortisone 75 to 150 mg daily is adequate

A trial of tincture of iodine in doses of 5 to 15 drops in a glass of water 3 times a day for 1 week out of 4 is recommended by some physicians as is gentian violet in 30 mg tablets 3 to 5 tablets every 24 hours or enough to color the stools blue

flamed diverticulum and drainage of the inflamed area, including drainage of complicating abscess Antibiotics should be tried

Idiopathic Dilatation of the Colon Hirschprung's Disease Megacolon

The first step in the treatment of this disease is to empty the bowel of its retained feces This should be done gradually by measures only mildly irritating to the mucosa of the colon First a rectal examination should be given to detect inspissated fecal material that may be present in the rectum If such is present manual removal may be necessary This should be followed by an enema of olive oil (150 to 180 cc), enough to fill partly but not distend the rectum often more oil than this is needed The enema should be retained for several hours if it does not precipitate a bowel movement It is well to repeat such an oil enema after a few hours Then there should be another rectal examination and if inspissated feces are felt they should be removed manually Cleansing enemas of warm normal saline solution should then be given, and they should be continued until the returned solution contains very little fecal material This procedure should be repeated several times at intervals of several hours

Early in the treatment the patient should be given a non bulky diet made up of food elements leaving but little residue in their digestive utilization Mineral oil by mouth is advisable Mild laxatives such as cascara or milk of magnesia are often helpful in clearing the colon of fecal contents when given in the dosage described under Constipation

With the colon once emptied of feces particularly after the removal of any inspissated feces or fecoliths from the rectum the patient needs to be put on a regime of low residue diet continued daily cleansing enemas and mild cathartics Under this program many patients can be kept in comfort without undue abdominal distension and without other treatment

It is important however after the colon has been emptied, to make an examination with anoscope and proctoscope to detect any local lesion that may be present as a contributory causative factor needing treatment After this x-ray study following a barium or other opaque enema should be carried out to detect any possible local lesion particularly one of obstructive nature whose treatment depending on its nature may become an important factor in the management of patients with

Anemia Anemia is frequent Since iron is often an intestinal irritant the anemia should be treated preferably by repeated small transfusions of blood — 300 to 500 cc each time

Mucous Colitis Irritable Bowel

Treatment consists of therapeutic measures appropriate to the management of anxiety neuroses and psychasthenia usually with the inclusion of psychotherapy with minimum attention to the bowels beyond the use of a non bulky low residue diet and the omission of cathartics colonic irrigations and enemas of all sorts except warm normal saline solution used infrequently The problem of constipation if it occurs is to be met as described in Chapter 1 If there are abdominal cramps and pain along the colon the use of a mild antispasmodic drug such as tincture of belladonna 10 to 15 drops by mouth 3 times a day or trasentine hydrochloride 75 to 150 mg by mouth 3 times a day will be helpful For many of these patients supplementary vitamins will be needed as described for Chronic Ulcerative Colitis

Diverticulosis Diverticulitis

Diverticulosis which is often demonstrated by x ray examination especially in older patients needs no treatment The too frequent practice of giving these patients oil enemas and frightening them by telling them a seed or other foreign body is apt to lodge in a diverticulum and cause serious trouble should not be continued Also the patient should not be frightened by being told he is likely to develop cancer in a diverticulum No dietary restrictions are necessary

If diverticulitis develops as it may and symptoms are mild a low residue diet should be used If the condition seems more severe bed rest low residue diet and oil enemas usually suffice to clear it up If there is fever and some leucocytosis it is desirable to give penicillin or aureomycin in dosage usually used in infections If there is obstruction hot applications to the abdomen bed rest semi starvation for a few days and oil enemas may relieve the obstruction If obstruction persists surgical exploration of the abdomen with probable colostomy is indicated If there is evidence of acute active inflammation treatment should be as for acute appendicitis with probable excision of the in

and, when this is true should be used Setting up exercises and exercises to strengthen the abdominal muscles with proper abdominal breathing are often useful adjuvants but exercise should stop short of more than slight fatigue An hour s rest, with the patient reclining and relaxed after the midday meal is advisable for many especially those who are fatigued by midmorning in some of these half an hour s rest before eating makes for a better appetite As many of these patients are underweight they should be given an appetizing diet of a nature to increase weight, but such a diet requires the best efforts of one skilled in dietetics

The neurosis and the nervous dyspepsia should be managed as are neuroses unassociated with visceroptosis Constipation should be managed as described under that heading These patients should get a minimum of drug therapy better no drugs at all Abdominal surgery should be refrained from unless there is evidence of organic obstruction of the intestine or of acute intra abdominal inflammation The physician should not tell or let anyone else tell the patient that there is a misplaced or too movable viscus the roentgenologist all too often in his fluoroscopic examination lets slip a remark that suggests a displaced or too movable organ has been visualized

Intestinal Obstruction

Intestinal obstruction from any cause should call for the institution of tube drainage both above and below the obstruction and prompt consultation with a surgeon If obstruction is not relieved promptly, surgical exploration is indicated with a probable ileostomy or colostomy above the obstruction and possible excision at this time or later of the involved intestine or the causative lesion, depending on the nature and cause of the obstruction

Constipation

Constipation is far more often an acquired habit than a disease This being so the most important way to treat it is by methods suited to breaking any acquired habit It is first of importance to obtain a complete history, including knowledge of the *patient's dietary* with his habits of eating and of occupation to make a careful physical examination and after this to educate the patient in what constipation is and

dilated colon It is inadvisable to give barium by mouth to these patients owing to the probable difficulty later of getting it out of the intestinal tract

With failure to find any type of locally obstructing lesion and with unsatisfactory results from the general methods so far advised drugs known to have a stimulating effect through the automatic nerve supply to the colon should be tried with the possibility that they may help by increasing colonic peristalsis Such drugs in their recommended dosages for adults are as follows acetyl beta methlycholine bromide (Mecholyl) orally in a dose of 0 1 to 0 2 gm 3 times a day after meals neostigmine (Prostigmine) bromide 15 mg by mouth 3 times a day Patients responding to these two drugs will usually receive better results when given the longer acting drugs of this group of which the following are good examples B methylcholine (Urecholine) chloride 5 to 10 mg for children and 10 to 30 mg for adults 3 times a day or carbaminoyl choline (Doryl) chloride 1 to 2 mg by mouth 3 times a day

Surgery has remained quite unsatisfactory in the management of dilated colon Lumbar sympathectomy has had some success Partial or complete colectomy has been used with occasional success If the sphincter ani is spastic dilating it manually or instrumentally may help In children Swenson s procedure — removal of a narrow irregular rectum and recto-sigmoid — has given good results Since it might possibly do so in adults it is worth trying If there is perforation of an ulcerated area with peritonitis surgery is imperative A demonstrated local obstruction will need surgical treatment For patients not responding reasonably well to medical therapy consultation with a skilled intestinal surgeon should be made available without undue delay

Visceroptosis

Many patients who are visceroptotic have no symptoms and need no treatment this is particularly true of those in whom the roentgenologist finds a misplaced viscus or misplaced viscera Of those with symptoms the majority have 4 indications for treatment (1) to treat the existing neurosis (2) to relieve the nervous dyspepsia (3) to overcome the constipation and (4) to reassure the patient by pointing out that the condition while unpleasant is in no way serious and that the position of the viscera and their mobility have no causal relation to their symptoms In some patients a well fitted abdominal support is comforting

Obviously the first thing to do in managing these patients is to find out whether they actually are constipated This can be done by persuading them to stop taking cathartics or a daily enema and observing what happens over a period of several days, possibly a week With this procedure the patient should include in his regular diet an intake of a considerable amount and variety of fresh fruit and green vegetables with water both at meals and between them The patient should go to the toilet as soon as he has the sensation of needing to move his bowels, possibly he should read or smoke while sitting on the toilet without straining to defecate After several days of no bowel movement it is wise for the patient to take in the morning after breakfast a fairly copious enema of warm normal saline solution, run in while he is seated on the toilet by introducting into the rectum a short, stiff nozzle affixed to a rubber tube extending from a rubber bag or glass enema receptacle fastened at shoulder level of the sitting patient A soft rubber rectal tube should not be used with the idea that it will reach up into the sigmoid and be more effective in washing out feces actually it often kinks on itself and its open end does not reach as high in the rectum as the stiff nozzle will The physician may need to convince the patient that the idea that enemas are harmful is a fallacy, a popular idea for which there seems no valid justification

After an enema as just described, the plan of again waiting a few days for a normal bowel movement should be tried, followed by the cleansing enema if needed Repetition of this procedure usually results in the patient s having a bowel movement at intervals of 1 to 3 days without use of either cathartic or enema This patient has been proved to be not constipated

The ideal way to have a minimum of bowel trouble is to respond promptly whenever a desire to move the bowels comes whether that comes at a regular hour daily or every other day sometimes even less frequently If the desire to move the bowels is not responded to promptly, later when the patient goes to stool probably no movement will follow Some patients can establish regularity in desire and hence regularity in bowel movements After breakfast is a period conducive to bowel movement and regularity without hurry often results then for many individuals In others this does not happen but by responding to desire whenever it comes these patients can be irregularly regular regular with respect to the day but irregular in daily time False modesty in women and business drive in both men and women often

why in him it is only an undesirable habit These patients should receive careful thorough and thoughtful consideration The physician must gain the patient s confidence and become sure that the constipation is not part of any general or local disease In order to exclude any local cause of constipation a thorough x ray study of the gastro intestinal tract should be carried out by a competent roentgenologist one who will not talk to the patient but will observe and report in detail his findings to the physician All too often some comment or remark to or over heard by the patient will very greatly increase his misgivings about con stipation Rectal examination and inspection through anoscope and sig moidscope are also desirable procedures of examination

The idea is very prevalent in America that a daily bowel movement is a necessity to normal living and that failure to have a bowel movement will produce abdominal distension and toxemia of serious con sequences In the treatment of constipation it is essential to disabuse the patient of these ideas by telling him of patients who are entirely healthy with a bowel movement not oftener than every second third or more days He should be told that constipation is not a cause of abdominal distension as witnessed by patients who normally have infrequent bowel movements with no distension and that feces stagnant in the bowel cause no toxic symptoms as shown by patients with idiopathic dilatation of the colon who with a bowel chronically loaded with feces have no toxemia What the patient thinks are symptoms of toxemia are not for they are relieved immediately by a bowel movement which is incompatible with toxemia if the symptoms are not so relieved they are caused by some condition like migraine not related to the constipation

The majority of patients seeking treatment for constipation are chronic users of nightly cathartic or morning enema if not of both They are habitues of anti constipation therapy and like drug addicts need to be broken of this habit Many of them unfortunately are neurotic in addition All of this complicates the problem of treating their believed constipation some of these patients seeking advice actually are not constipated A patient passing daily or every other day a small stool because of a small food intake all the items of it low in residue is not constipated This is also true of those who have only a small bowel evacuation or none at all for a day or so after vigorous catharsis Some individuals normally have not a daily stool but one every second or third day occasionally only after longer intervals

satisfactorily effective Patients vary greatly in regard to the kind of laxative that will work best and which will continue to work over very long periods of time without need of increasing dosage or changing to another Testing by trial of several may be necessary If a patient by long use has found a given laxative productive of regular, not too soft or fluid stools, and is unwilling to go to the trouble of learning how not to need a laxative then the part of wisdom is for the physician not to change the patient's cathartic Usually these patients do not consult the physician because of constipation The ones that do are those who have not found a satisfactory laxative or those whose favorite laxative has ceased to give satisfactory results First the physician must find out if something has developed to cause this change and what it is He may find that now there is something more important than constipation that needs medical or possibly surgical treatment

There are many laxative drugs available for the treatment of simple constipation in the patient unwilling to take the time for, and give the effort to learning how to have bowel regularity without using a drug or enema A popular one is mineral oil alone or in combination with agar, without which the oil sometimes leaks through the rectum It should be given in 15 to 30 cc doses once or twice a day before eating Mineral oil has the disadvantage of hindering absorption of food stuffs especially fat soluble vitamins, A D, and K and in debilitated patients it may be regurgitated and enter the lung to cause pneumonia Another popular laxative is prunes cooked with the addition of 2 or 3 gm of senna to 6 large prunes, the patient eating from 4 to 6 of these prunes at breakfast Cascara sagrada in some of its forms such as aromatic fluid extract 2 to 6 cc fluid extract, 1 to 3 cc or powder 0 1 to 0 3 gm in a pill or tablet is a very satisfactory laxative for prolonged use Milk of magnesia 15 to 20 cc is also excellent All of these should be given at bedtime Phenolphthalein is not advised as it is often too irritating and may be seriously toxic Sodium phosphate 4 to 8 gm dissolved in hot water and taken before breakfast, is one of the milder saline cathartics for occasional use Bulk producers such as methyl cellulose (Cellothyl) in doses of 1 0 to 4 0 gm will often give good results With the use of any of these laxatives an effort should be made to reduce gradually the dose being given in the hope of getting even this type of patient freed from the habitual use of cathartics

As has been stated already enemas can be used without any harmful effects and may be needed each morning or at least often by some of

act to prevent this irregular form of regularity In the final analysis if all could and would respond whenever the desire for a bowel movement comes constipation real or imaginary would largely cease and there would be many more people who would never have to use a cathartic or enema

Another popular fallacy is that exercise is necessary to bowel movement but there are many bedridden patients and others necessarily almost always sedentary who have regular bowel movements without cathartic or enema while those overtired from exercise taken as conducive to bowel movements are often unable to move their bowels until they have had a long period of rest to overcome their exercise induced fatigue This is not to say that exercise not overdone exercise that is a part of good hygiene is undesirable so far as bowel habits are concerned

Straining at stool should always be condemned for the bowels will move without straining and straining causes a rise in blood pressure and is conducive to the development of hemorrhoids which in themselves not infrequently contribute to causing or perpetuating constipation

As already intimated a nutritious diet with a large moiety of bulky foods such as fresh fruits and green vegetables which leave a considerable undigested unabsorbable residue, should be taken by patients having difficulty in attaining regularity of bowel movements Some find a high fat diet oo gm per day conducive to regularity For others more starchy food such as potatoes have the same effect Increase in fluid intake helps others Any diet however must be appetizing not disturbing to gastric function and not causative of intestinal irritation if its use is to be kept up In these respects so called roughage diets chiefly diets with much bran may be injurious In some however they do work well and should be used The daily use of bran is not advised

However there are many individuals who after the physician has done his best in education and diet planning and even after they have been freed from the use of cathartics will refuse to maintain regularity of bowels without cathartics or enemas and the best the physician can do is to guide their choice of cathartics so that they will not get in the *habit of using ones that are drastic i e too irritating to the bowel and* causing watery bowel movements instead of the ideal solid or even semi solid ones

Mild laxatives are to be used the milder the better so long as they are

4 KIEFER E D Evaluation of Clinical Management of Chronic Ulcerative Colitis *Gastroent*, 1948 x p 16
5 KIRSNER J B and PALMER, W L Effect of Corticotropin (ACTH) in Chronic Ulcerative Colitis" *Jour Amer Med Assoc*, 1951 CXLVII p 541
6 MACHELL A T E and HOLLAN O R The effect of Cortisone on the Clinical Course of Chronic Regional Enteritis and Chronic Idiopathic Ulcerative Colitis *Am Jour Med Sc*, 1951, CCXXI p 501

Hirschsprung's Disease

1 SWENSON O RHEINLANDER H and DIAMOND I 'Hirschsprung's Disease New Concept of Etiology Operative Results in 34 Patients *N E J Med*, 1949 CCXLI p 551

Constipation

1 BARGEN J A Method of Improving Function of the Bowel Use of Methylcellulose *Gastroent*, 1949, XIII, p -75

the patients with constipation sometimes even by those taking a nightly laxative It is wise to use only the very mild enemas such as warm saline solution or tap water in preference to a more irritating one Rarely if feces become inspissated or impacted an oil enema of 150 cc retained over night will be needed to soften the fecal material so that it can be washed out next morning with a cleansing enema of warm saline solution or tap water

As has been intimated already many of the patients with the cathartic or enema habit have neuroses Such neuroses should be treated as any other form of neurosis and their treatment made an important part of the management that seeks to restore to normality the patient s bowel habits

Tumors

Tumors in any part of the small or large intestine should be removed surgically unless already extensive metastasis is in evidence Even then there may be symptoms of obstruction which call for prompt surgical *treatment to end the obstruction and if possible to remove the ob*structing neoplasm The needed pre operative tube drainage is discussed in the section on intestinal obstruction A steadily increasing number of tumors of the intestine are being diagnosed successfully before matastasis or regional extension takes place and many of these can be removed completely and quite a few do not recur or metastasize This is true more often of neoplasms of the large than of the small intestine

BIBLIOGRAPHY

Chronic Ulcerative Colitis

1 BATES C S An Inquiry into the Surgical Treatment of Ulcerative Colitis *Am Jour Med Sc* 1951 ccxxii p 211
2 ELLIOTT J M KIEFER F D and HURXTHAL L M The Treatment of Chronic Ulcerative Colitis with Pituitary Adrenocorticotrophic Hormone (ACTH) *N E J Med* 1951 ccxlv p 288
3 GRAY S J REIFENSTEIN R M and BENSON J A ACTH Therapy in Ulcerative Colitis and Regional Enteritis *N E J Med* 1951 ccxlv p 481

Cirrhosis of Liver

Portal Cirrhosis The treatment of portal cirrhosis has undergone a marked improvement during the last 10 years and now, instead of the former almost hopeless prognosis, an increasing number of cases respond quite satisfactorily to therapy

Patients should be placed on complete bed rest and maintained at rest until tests of liver function show that physical activity does not impair liver function Too early or too much activity, increasing the general metabolic demands on the liver, can be harmful and should be carefully avoided

Any alcoholic consumption should be stopped and active measures taken to insure against future alcoholic intake Psychiatric evaluation and psychotherapy are necessary, if the usual lapse to alcoholic consumption is to be avoided Thorough co-ordination among the internist, psychiatrist, dietitian, and social-service worker is essential to successful treatment in many of these cases

Diet therapy should be commenced promptly Careful check on the food tastes, desires, dislikes, and habits of the patient is important, and the information thus gained must be applied in preparing a palatable diet It is essential that the patient eat the food prepared for him—which can be accomplished only by making use of every possible means to encourage and help him The anorexia, so common in these patients, may make force-tube feeding necessary in spite of the best efforts to get them to take food by mouth Whenever possible, food should be given by mouth, since oral feeding is in many ways much more satisfactory than tube feeding However, oral feeding should not be carried out at the expense of nutritional loss The diet, consisting of approximately 3500 calories, should contain about 145 gm protein, 350 to 500 gm carbohydrate, and sufficient fat, usually 150 to 160 gm, to make it palatable It should supply abundant amounts of meat, milk, eggs, fruit, and green vegetables The diet on the following page illustrates a satisfactory one In the presence of severe liver failure with impending coma, proteins must be withheld since in this state they are definitely toxic and can force a patient into hepatic coma

Careful check must be made and records kept of the amount of food actually consumed If insufficient calories or essential nutriments are being ingested, tube feeding may be necessary

Skimmed-milk powder and brewers' yeast may be utilized to supply

CHAPTER XLI

DISEASES OF THE LIVER BILE PASSAGES AND GALL BLADDER

Abscess of the Liver

The treatment of amebic abscess of the liver is described under Amebiasis

Suppurative pylephlebitis and pyemic abscesses should receive chemotherapy with the proper antibacterial agent as soon as the diagnosis is made and the sensitivity of the causative agent is determined Early vigorous chemotherapy with penicillin streptomycin chloromycetin aureomycin or terramycin depending on organism sensitivity has improved markedly the prognosis in these serious infections A high calorie high carbohydrate high protein low fat diet richly supplemented with vitamins especially those of the B complex should be given Patients should be on complete bed rest Surgical drainage is indicated if the chemotherapy does not eliminate the infection

Amyloid Liver

The treatment for this condition is for the most part supportive Chronic infection such as old osteomyelitis tuberculosis or other pyemic processes if they are in an accessible area should be eradicated either by vigorous chemotherapy or by surgical removal Recent observations in several clinics indicate that in early amyloidosis of the liver there is *definite regression if the patient is given large amounts of raw* liver 300 to 400 gm by mouth daily The liver is prepared by grinding it through a fine meat chopper and pressing it through a sieve It is then given in 1 dose between meals in tomato juice grapefruit juice ginger ale or other palatable preparation

a portion of the protein These may be added to soups, milk, or fruit juice as desired Brewers' yeast powder prepared in an eggnog and seasoned to the patient's taste is a good source of protein and also supplies other essentials Usually 25 gm twice a day is sufficient It is unpalatable to some patients and causes distention or diarrhea, in these cases it should be replaced by skim-milk powder Since nearly all cirrhotic patients have an associated deficiency, the diet of those unable to take yeast should be supplemented with purified vitamins until these deficiencies have been controlled Usually a daily vitamin supplement of 5 times the normal requirement is satisfactory When there is poor absorption of fat-soluble vitamins, such as occurs in the presence of jaundice, vitamin K [menadione sodium bisulfite], 2 to 4 mg, should be administered parenterally daily until the prothrombin level is normal and remains so Patients exhibiting neuritis or signs of central nervous system involvement should receive at least 25 mg of thiamine hydrochloride and 100 mg of nicotinamide intramusculary 3 times a day Unconcentrated liver extract (Intraheptol), 5 cc, should be given twice weekly

If the patient consumes the full diet previously outlined, he will have a sufficient supply of lipotropic factors However, in a cirrhotic patient exhibiting severe dietary deficiency or in one not responding satisfactorily to therapy, they should be supplied in pure form until sufficient amounts of these factors can be furnished by the diet For this purpose choline chloride or choline dihydrogen citrate, 0 5 gm 3 times a day is satisfactory The substitution for the choline of methionine, 1 to 2 gm 3 times a day is also effective

Anemia if macrocytic in character may be ameliorated by adequate liver or vitamin B_{12} therapy as described under Pernicious Anemia There is often an associated iron deficiency anemia, however, which will require 1 to 2 gm daily of ferrous sulfate or, if a less irritating iron is needed, ferrous gluconate Severe anemia not responding to therapy or resulting from hematemesis or chronic blood loss requires blood transfusion

Patients in severe hepatic failure or with cholemia should be given intravenous infusions of 10 per cent dextrose containing 50 mg thiamine hydrochloride, 100 mg nicotinamide and 20 mg of riboflavin - or 3 times daily Infection dehydration, acidosis, acute blood loss, or other factors complicating or precipating the cholemia should be corrected promptly Oral or tube feeding should be begun as promptly as possible

SAMPLE DIET FOR CIRRHOSIS

Breakfast Fruit juice orange grapefruit tomato 1 glass
Cereals cream of wheat oatmeal wheatena 1 saucer
Toast slices
Egg 1
Butter 1 pat
Sweet jelly jam marmalade 1 tablespoonful
Milk 1 glass
Coffee with cream and sugar

10 a m feeding Eggnog — 1 egg 1 glass milk sugar to taste dash of cinnamon or nutmeg to taste, add 25 gm of yeast or of milk powder if patient finds yeast unpalatable

Noon meal Meat lean meat chicken liver fish moderate serving
Vegetables 1 serving asparagus green beans lettuce squash or tomatoes
1 erving carrots peas lima beans or turnips
1 serving corn, kidney beans potatoes or rice
Bread slices
Butter 1 pat
Dessert cake pudding fruit 1 serving
Milk 1 glass
Coffee with cream and sugar

2 p m feeding Eggnog as at 10 a m

4 p m feeding Fruit juice orange prune cranberry et cetera well sweetened

Evening meal Meat as at noon
Vegetables celery lettuce tomato radishes carrots as salad 1 serving of beans corn pota toes rice
Bread 1 slice
Butter 1 pat
Milk 1 glass
Fruit bananas figs prunes pears apples blue berries et cetera
Tea with cream and sugar

8 p m feeding Milk 1 glass
Cottage cheese 1 tablespoonful
Soda crackers 3

until the individual patient's tolerance for it has been established If bleeding has occurred from esophagal varices, anticoagulant therapy should not be employed

Other Cirrhoses Cirrhosis resulting from acute or subacute hepatic necrosis, hemachromatosis, biliary disease, syphilis, cardiac failure, capsular hepatitis, or perihepatitis or so-called hypertrophic cirrhosis should receive treatment similar to that outlined for portal cirrhosis in addition to specific measures directed against the causative factor, if such is known

Various *surgical procedures* have been devised for the relief of ascites, portal hypertension, and esophageal varices These include omentopexy, anastomosis of the splenic vein to the renal vein, splenectomy, peritoneal button, ligation of the coronary vein of the stomach, and injection of the esophageal veins with sclerosing agents A limited degree of success in properly selected patients may be obtained, but for the most part surgical treatment is unsatisfactory

Hepatitis

Hepatitis produced by various toxic agents such as arsenicals, carbon tetrachloride, tetrachlorethane trinitrotoluene, benzene, picric acid, diethylenedioxide [Dioxan], dinitrophenol, phosphorus, and other hepatotoxic agents should be treated in much the same manner as that recommended for viral hepatitis A high-protein, high carbohydrate diet, abundantly supplemented by vitamins of the B complex as described for Portal Cirrhosis, is indicated In acute cases with fatty infiltration of the liver, when the patient is not taking an adequate diet, the administration of choline chloride 0 5 gm 3 times a day, or methionine, 1 to 2 gm 3 times a day, may prove helpful

Absolute, often prolonged bed rest is essential, and if nausea and vomiting preclude oral fluids and nourishment, daily intravenous glucose, 2 or 3 liters of a 10 per cent solution, should be given If there is loss of chloride, or if acidosis develops, sufficient physiological sodium chloride solution must be given to maintain normal values Hepatitis caused by arsenicals should receive dimercaprol (BAL) as described under Arsenical Poisoning Vitamin K [menadione sodium bisulfite], 2 to 4 mg parenterally is indicated if prothrombin values fall or hem-

Edema and ascites should be relieved as quickly and as completely as possible Abdominal paracentesis should be performed at sufficiently frequent intervals to avoid abdominal distention Fluid should be permitted in sufficient amounts to relieve thirst and supply the normal desires of the patient Usually 2000 cc will prove sufficient Sodium chloride should be restricted moderately in the usual case The avoidance of its use in cooking and the seasoning of food on the table is usually a sufficient restriction The more severely edematous patients will require greater salt restriction This may be accomplished by selecting foods low in sodium content as well as by restricting the salt used in the cooking and seasoning of food Ammonium chloride administered as 0 5 gm enteric coated pills 2 gm 3 times a day after meals, 48 hours before the intramuscular administration of mellurde (Mercuhydrin) 1 to 2 cc will be helpful in eliminating and preventing the reaccumulation of ascites Usually 2 or 3 weekly injections of the diuretic are satisfactory Occasionally mellurde 1 0 cc intramuscularly daily for a few days combined with ammonium chloride 6 gm daily is required to obtain the best results Care must be taken when the diuretic is given in this manner since excessive sodium chloride and calcium may be lost There is also danger of mercury poisoning if there is oliguria Intravenous infusions of 25 to 50 gm of salt poor albumin solution on alternate days may be helpful Larger doses up to 50 to 100 gm may be given to severe cases with good effects It must be given with some caution however for acute pulmonary edema can result

Patients must receive expert nursing care Great effort should be made to encourage full dietary intake At the first indication of intercurrent infection adequate chemotherapy should be instituted

Restless patients may require mild sedation It is important to remember that toxic effects may result from sedatives or narcotics metabolized by the liver Small repeated doses should be given until the patient s tolerance is known Phenobarbital pentobarbital or barbital in approximately half the commonly prescribed doses is usually sufficient Morphine and other narcotic drugs should be avoided or given in small dosage until tolerance is ascertained Usually a fourth the usual dose is safe initially

If phlebitis occurs it should be treated with heparin or bishydroxy coumarin (Dicumarol) as described for Coronary Occlusion Care must be exercised in the dosage of the drug in this group of patients

adryl) hydrochloride, tripelennamine (Pyribenzamine) hydrochloride, 50 mg 3 times a day orally, or 2 per cent tripelennamine (Pyribenzamine) hydrochloride ointment to the skin are recommended Slow intravenous injections of 20 cc of a 0 1 per cent procaine hydrochloride may also give relief Ergotamine tartrate, 1 0 mg, twice a day may be helpful also A 10 per cent solution of calcium chloride or calcium gluconate in an intravenous dose of 10 cc may be helpful Occasionally sedatives and analgesics are required If hemorrhage occurs, vitamin K [menadione sodium bisulfite], 2 to 4 mg, should be given intramuscularly or intravenously daily until prothrombin time is normal, then the dose should be reduced to 1 mg daily or as often as required to keep the prothrombin time normal Occasionally the symptoms of pruritus clear as an obstructing lesion is relieved by external drainage of bile salts from a T tube placed in the common bile duct

Acute Cholangitis

Treatment is directed mainly toward preparing the patient for surgical drainage, since mechanical obstruction by a stone, tumor, or constricting band is usually the underlying lesion Patients should be in bed receiving at least 3000 cc of fluid daily, and the diet should be a bland one Heat or cold, whichever gives more comfort, may be applied to the painful area If pain is severe, methadone hydrochloride, 5 to 10 mg, meperidine (Demerol) hydrochloride 100 mg or morphine sulfate, 8 mg, at 3- or 4 hour intervals for 3 doses, is helpful Colicky pain may be relieved also by giving intravenously 10 per cent calcium gluconate solution, 10 cc, by inhalation of amyl nitrite 0 3 cc, by a sublingual dose of glyceryl trinitrate [nitroglycerin] 0 6 mg, or by aminophylline 0 5 gm intravenously If there is much restlessness sodium barbital 0 3 gm, or phenobarbital, 0 1 gm may also be given Penicillin and streptomycin, or intravenous aureomycin chloramphenicol, or terramycin should be given a therapeutic trial, but if fever, pain, and leukocytosis do not decrease promptly or if they increase immediate surgical intervention is indicated

Cholecystitis

Acute cholecystitis is primarily a surgical condition and surgical in

orrhage occurs Severe anemia may require blood transfusion Iron and occasionally liver are helpful if a chronic anemia is present

None of the antibiotics except possibly terramycin, has proved very helpful in the treatment of hepatitis With the presence of fever leukocytosis and increased sedimentation rate terramycin 500 mg 4 times a day, may be tried The administration of Corticotropin cortisone, or similar acting steroid hormones in the treatment of viral hepatitis has given variable results Some evidence suggests that in the acute stage Corticotropin given 10 days or more after onset may be more beneficial than when given early yet it may give rise to hyperglycemia and glycosuria Corticotropin given in the acute stage may speed up the return of certain clinical laboratory and pathological features toward normal at the same time it may leave the patient more vulnerable to relapse than patients not given Corticotropin Decrease in serum bilirubin levels during steroid hormone therapy may be due largely to their choleretic action on the liver In more severe cases of hepatitis both Corticotropin and cortisone similarly may give temporary improvement with a tendency to relapse, in fulminating cases these agents seem to be of little or no benefit

If renal involvement occurs in conjunction with the hepatitis as in carbon tetrachloride poisoning the nephritis should be treated as described under Diseases of the Kidney

Acute yellow atrophy may develop as a consequence of severe hepatitis Treatment of this condition is much the same as that described previously for acute hepatitis except that large amounts of fluids should be given to assist in eliminating the toxic agent Abundant intravenous glucose solution should be supplied As recovery occurs, these cases should be treated as described under Portal Cirrhosis

Jaundice

Treatment of the symptoms of jaundice is unsatisfactory Therapy for the most part should be directed toward relieving the causative factor The pruritus produced by jaundice may be most annoying and present a difficult therapeutic problem Warm alkaline baths sponging with a solution of sodium bicarbonate or of equal parts of vinegar and water or a 1 to 2 per cent solution of phenol application of 5 per cent menthol ointment, antihistaminic drugs such as diphenhydramine (Ben

A simple bland diet, such as that recommended in the treatment of duodenal ulcer or irritability of bowel, should be given Spiced and highly seasoned foods should be avoided If fats do not definitely create distress, they may be permitted in moderate amounts in the diet It is doubtful that much is to be gained by rigid fat restriction, but since these patients are usually overnourished and apparently do not handle cholesterol well, it is wise to reduce the intake If dyspepsia is a symptom, 1 teaspoonful of a mixture of equal parts of sodium sulfate, sodium phosphate, and sodium bicarbonate in half a glass of water 3 times a day often gives considerable relief If constipation is present, 2 to 3 teaspoonfuls of sodium phosphate in hot water, or 2 teaspoonfuls of magnesium sulfate, before breakfast will usually correct the condition satisfactorily In chronic cases and in those with gastric or bowel irritability, milk of magnesia, 15 to 30 cc before breakfast or at bedtime, is soothing and effective

Antispasmodics are often helpful in these cases Atropine sulfate, 0 4 to 0 6 mg, 1, hyoscyamine (Bellafoline), 0 25 to 0 5 mg subcutaneously or tincture of belladonna, 0 6 cc to 1 3 cc by mouth 2 or 3 times a day, may give considerable relief Acute episodes of pain, possibly resulting from spasm of the sphincter of Oddi, may be relieved by the inhalation of amyl nitrite Nitroglycerine, 0 6 mg dissolved under the tongue every 4 hours, is also effective in relieving spasm and may prove most helpful in patients having chronic discomfort from spasm of the sphincter or gall bladder Occasionally trasentine hydrochloride, 75 to 150 mg orally or 50 mg intravenously or intramuscularly, will prove helpful Phenobarbital, 15 mg 3 or 4 times daily during periods of stress, is soothing

Bile preparations such as bile salts, 0 2 to 0 4 gm 3 times daily after meals, may be beneficial

Stimulation of biliary drainage by intubation and instillation of magnesium sulfate in the duodenum is of questionable value The fat of the diet will give a more adequate stimulation and afford more effective drainage

Not infrequently psychotherapy gives striking results in these cases when all else fails to relieve

Chronic cholecystitis, occurring in the presence of a poorly or nonfunctioning gall bladder, is treated as just described when the attacks are mild or when surgery is contraindicated These patients are much more likely to have recurrences and progression of the disease leading

tervention is usually indicated as soon as the patient is in a suitable phys ical state Medical therapy should be directed toward preparing the patient for operation and carrying him through the acute phase until he is in a more satisfactory condition The decision to operate depends on many factors but generally recurrent attacks and severe attacks should be treated surgically as soon as the patient s condition warrants it Once the diagnosis is made, the patient should be placed in bed with the head of the bed elevated from 8 to 12 inches Fluids should be given to correct any dehydration Three liters of physiological saline con taining 5 per cent glucose, given intravenously daily, are usually suffi cient Inhalation of amyl nitrate or glyceryl trinitrate [nitroglycerin], 0 25 to 0 6 mg sublingually, may relieve associated spasm Calcium chloride or calcium gluconate 10 cc of a 10 per cent solution or amino phylline 0 5 gm given intravenously, will frequently relieve colicky pain If no relief is obtained by their use, morphine sulfate 8 mg or meperidine (Demerol) hydrochloride 50 to 100 mg intramuscularly may be helpful Methadone hydrochloride, 5 to 10 mg intramuscularly or orally, may prove even better If there is considerable restlessness, seda tion with sodium barbital, 0 3 gm, or phenobarbital, 0 1 gm is indicated Hot or cold packs according to the patient's preference applied to painful areas are also helpful

Chemotherapy should be given Penicillin alone or combined with streptomycin, is undoubtedly helpful in preventing the development of liver abscess and certainly is of value in the treatment once an abscess has formed

Careful observation should be made of the temperature pulse white blood cell count and muscle spasm If they subside surgery may be delayed until the acute episode is over If on the other hand they increase surgery may be necessary in spite of the acute condition of the patient Surgical removal of the gall bladder coupled with careful exploration of the common duct usually gives complete and permanent relief Sometimes cholecystostomy is advisable

Chronic cholecystitis in the absence of demonstrable gall stones or marked impairment of gall bladder function should be treated conserva tively unless attacks are severe or frequent The true nature and origin of the symptoms are often confusing and consequently medical therapy should be given before resorting to surgery Surgery is not infrequently unsuccessful in relieving symptoms in these cases, particularly if no stones are present

2 SCHWARTS R PHILLIPS G B, STEEGMILLER, J E GA BUZDA, G J, and DAVIDSON, C S 'Dietary Protein in the Genesis of Hepatic Coma, *N E J Med*, 1954, CCLI 685

Hepatitis

1 WATSON, C J, and GREENBERG, A, 'Certain Effects of Salt Poor Human Albumin in Cases of Hepatic Disease' *Am Jour Med Sc*, 1949, CCXVII p 651
2 HAVENS W P Jr "Infectious Hepatitis" *Medicine*, 1948, XXVII p 279
3 PHILLIPS R W 'Low sodium Diet in Management of Ascites *Arch Int Med*, 1951, LXXXVII, p 636
4 WELCH C S 'Portal Hypertension" *N E J Med*, 1950 CCXLIII p 598
6 WATSON C J The Prognosis and Treatment of Hepatic Insufficiency *Ann Int Med*, 1949 XXXI, p 405
7 MULTIPLE AUTHORS Symposium on Viral Hepatitis,' *Am J Med*, 1950 VIII p 559
8 COLBERT J W Jr HOLLAND, J F, HEISSLER, I and KNOWLTON, M 'The Use of ACTH in Viral Hepatitis,' *N E J Med*, 1951 CCXLV, p 172
9 EVANS A S SPRINZ H, and NELSON, R S 'Adrenal Hormone Therapy in Viral Hepatitis I The Effect of ACTH in the Acute Disease II The Effect of Cortisone in the Acute Disease, III The Effect of ACTH and Cortisone in Severe and Fulminating Cases *Ann Int Med*, 1953, XXXVIII 1115 1134 1148
10 PATTERSON P R, DINGMAN J F, SCHWACHMAN H and THORN G W Choleretic Action of Cortisone," *N E J Med*, 1954 CCLI 502

Cholecystitis

1 BUXTON R W RAY D K and COLLER F A Acute Cholecystitis *Jour Amer Med Assoc*, 1951 CXLVI p 301
2 MONROE R T *Diseases in Old Age*, Harvard University Press 1951, p 210

Tumors

1 LEVENSON, R N and MASON, D G 'Mixed Adenoma (Hamartoma) of the Liver *Ann Int Med*, 1953, XXXVIII 136
2 SANFORD C H Primary Malignant Disease of the Liver, *Ann Int Med*, 1952 XXXVII 304

ultimately to surgery In those chronically ill with recurrent attacks it is usually wise to remove the damaged gall bladder as soon as there is a favorable opportunity If it is left alone, cancer may follow

Chronic cholecystitis occurring in the presence of gall stones, when mild, will usually respond well to medical therapy as just outlined However, there is always the possibility of severe infection, obstruction, or perforation of the gall bladder or a secondary pancreatitis In patients suffering repeated attacks of colic and jaundice with general ill health the gall bladder should be removed surgically The operative mortality in properly selected patients is small and most certainly less than when the surgery is done under unfavorable circumstances Medical treatment should be reserved for those in whom surgery is contraindicated and for those with mild, single, or widely separated attacks

Cholelithiasis

Cholelithiasis with severe biliary colic should be treated as described under Acute Cholecystitis Patients with mild colic or more chronic symptoms should be treated as outlined for cholecystitis with stones

Tumors of the Liver

A mixed adenoma (hamartoma) of the liver, although rather rare, not infrequently is circumscribed and encapsulated and thus may be resectable surgically

A primary tumor of the liver, a hepatoma rather rare in the white race, but more common in the yellow race, is often not as resectable as a hamartoma yet when removal of a greater portion of it can be carried out such a procedure may prolong the patient s life

BIBLIOGRAPHY

Cirrhosis of Liver

1 GOODYEAR, A V N REIMAN A S LAWRASON F D and EPSTEIN F H Salt Retention in Cirrhosis of the Liver *Jour Clin Invest*, 1950 xxix, p 973

The drug may be given orally, or through a gastric tube, 0 5 gm every 6 hours, or intravenously if necessary, 0 5 to 1 0 gm every 12 hours

Surgical Treatment It is best to have a surgical consultant in attendance, but unless there is doubt about the diagnosis, surgery is not indicated It has been demonstrated clearly that a previous mortality of 30 per cent following surgical treatment in uncomplicated acute pancreatitis has been reduced to 15 per cent by the non-surgical conservative measures just outlined On the other hand, if a history of duodenal ulcer is obtained, and it is suspected that perforation of the ulcer into the pancreas has occurred, an operation should be performed Likewise, after recovery from the acute attack, if signs of suppuration and abscess-formation develop, surgical drainage should be carried out. Lower thoracic, paravertebral, sympathetic nerve block of the sphincter of Oddi may be helpful for the severe pain caused by spasm

After 48 to 72 hours of the medical management as just outlined, liquid foods by mouth may be introduced gradually, while the gastric suction is clamped off, until more solid foods can be tolerated and the gastric drainage tube removed During this interval atropine sulfate, 0 40 to 0 60 mg hypodermically 3 or 4 times a day may be helpful

Following complete recovery, a careful x-ray study should always be made for cholecystitis and duodenal ulcer Pancreatitis secondary to duodenal ulcer is apt to be a suppurative process and will require surgical drainage and closure of the ulcer as already mentioned Thereafter strict medical management of the ulcer should be carried out Where gall-bladder disease is found to be present, medical management may be carried out in the absence of stones but usually it is wisest, after an acute attack of pancreatitis, to remove the gall bladder When an alcoholic debauch has precipitated the attack of acute pancreatitis, simply calling this fact to the attention of the patient may be sufficient to prevent him from repeating the experiences of such an acutely painful and frequently lethal illness, and in this sense informing him becomes a form of prophylaxis

Chronic Pancreatitis The treatment of chronic pancreatitis is not often very satisfactory, for diagnosis may be difficult, medical therapy prolonged and insufficient, and surgical therapy may become inevitable A nutritious diet high in carbohydrate, low in fat, adequate in proteins and high in calcium content should be instituted Protein hydrolysates should supplement the natural proteins if achylia is present Calcium salts, 0 5 gm, 2 tablets after each meal should be given to replace the

CHAPTER XLII

DISEASES OF THE PANCREAS

Pancreatitis

Pancreatitis whether acute or chronic is seldom due to an inflammation but results most commonly from an autolytic process which is spoken of as tryptic digestion, leading to manifestations of pancreatic insufficiency

Acute Pancreatitis Usually acute pancreatitis is secondary to (1) gall bladder disease (2) chronic alcoholism or (3) duodenal ulcer penetrating into the gland substance It may be cryptogenic These contributory disorders must be given therapeutic consideration after the acute episode of pancreatitis has subsided

The patient is acutely ill often in shock Complete bed rest is imperative with the foot of the bed elevated 10 to 12 inches and the patient kept warm with blankets Since pain is usually severe morphine sulfate 8 to 15 mg subcutaneously should be given at once Atropine sulfate 0.6 mg subcutaneously and aminophylline 0.5 gm intravenously may aid in relieving spasm Methantheline (Banthine) bromide, 100 mg parenterally every 6 hours may be helpful To restore circulating blood volume immediately 1 to 2 pints of blood plasma should be given intravenously When anemia is present whole blood should be substituted for the plasma Continuous gastric suction through a Wangensteen tube should be instituted while withholding all food and fluids by mouth Give 5 per cent glucose in normal saline solution intravenously to maintain fluid and electrolyte balance If the blood calcium level is low, 1.0 gm of calcium gluconate should be given intravenously and repeated as needed With associated complications of the biliary tract and for the prevention of secondary infection antibiotic therapy should be given Since the tetracyclines are concentrated in the bile they are perhaps the antibiotics of choice under these circumstances

terized by gross deficiency or absence of the secretion of the pancreatic juice with resulting poor digestion of protein, starch and fats, and the development of lesions of the liver, kidneys and lungs, has a more favorable prognosis with treatment today than it had a few years ago Proper dietary therapy is of the first importance, with control of respiratory infections, bronchitis, pneumonia, and sometimes bronchiectasis, and is essential for continued health and adequate growth

Protein, though poorly utilized, is well tolerated and double the normal requirement should be given The fat content should be low with care being taken to provide essential food substances which are fat soluble The *carbohydrate* intake should be high to compensate for the lack of calories from fat Vitamin supplements should be added

These principles are embodied in the following diet outline suggested by Andersen

Infants under 6 months Formula per kilo of body weight Protein milk powder 20 to 25 G glucose 15 gm, Amigen 2 gm, water 180 c c Supplements per day Pancreatin 0 5 to 1 0 gm, per bottle, oleum percomorphum 12 to 40 drops, ascorbic acid 50 mg, vitamin B complex Solid food Add egg yolk and mashed banana at 6 to 8 weeks, pureed cooked fruit at 12 weeks, meat, jello, junket at 5 to 6 months

Infants 6 to 12 months Formula, per kilo of body weight, Protein milk 15 to 20 gm, cane sugar or banana powder 8 gm, water 125 to 150 c c At 8 to 12 months this may be changed to skim milk with cane sugar added in amounts of 60 gm per 1000 c c Supplements Pancreatin 1 5 gm (1 teaspoonful) per meal, oleum percomorphum 15 drops three times a day, ascorbic acid 50 mg, vitamin B complex

Breakfast 2 to 4 ounces of fruit juice, 1 egg, 1 slice of zwieback, 1 mashed, ripe banana, 6 to 8 ounces of formula, 1 level teaspoon of Pancreatin

Dinner 1 to 2 tablespoons or more of minced lean meat, 1 to 2 tablespoons or more of pureed vegetables dessert, pureed cooked fruit gelatin or junket, formula, Pancreatin

Supper Similar to dinner, with pot cheese instead of meat, the pot cheese may be flavored with honey jelly, or banana powder

Evening Formula and if desired banana

Children over one year The following additions are made one by one One serving of cereal bread or potato per meal Fish may be substituted for meat Hard candy and marshmallows, fruit ices, cake without fat (sponge and angel food), chopped vegetables, and later any form of

calcium being lost in the stool Pancreatin, USP 0 3 gm, 1 to 3 enteric coated tablets should be given after each meal to replace deficient pancreatic enzymes To aid impaired calcium and fat absorption sorbitan mono-oleate (Tween 80) a detergent agent may be tried in doses of *1 5 gm 3 times daily for adults and for children 1 0 gm daily with* meals Dilute hydrochloric acid, 7 0 to 10 0 cc in a glass of water, taken through a glass tube with meals should be given particularly if achylia gastrica accompanies the pancreatic disorder

The severe pain sometimes encountered may require repeated hypodermic injections of morphine sulfate, 8 to 15 mg Some prefer to use meperidine (Demerol) hydrochloride 50 to 100 mg hypodermically Atropine sulfate 0.40 to 0 60 mg hypodermically 3 or 4 times a day may be helpful in combating the chronic epigastric distress so often present Supradiaphragmatic splanchnicectomy may be helpful for the chronic pain

If continued study indicates surgery, the procedure should be highly individualized with sphincterotomy vagotomy partial gastrectomy or biliary shunts carried out as may be indicated in the particular case

In the interacinar type of chronic pancreatitis there is apt to be glycosuria which should be treated with insulin in the same way as outlined under Diabetes Mellitus In this circumstance the diet outlined *in a preceding paragraph may have to be modified by lowering* the carbohydrate allowance for the proper control of the glycosuria

Since chronic pancreatitis is also frequently secondary to disease in the hepatobiliary system or gastro intestinal tract careful search for hepatitis cholecystitis and duodenal ulcer should be carried out and proper measures instituted toward their correction If obstruction of pancreatic ducts is present as the cause of the chronic pancreatitis *surgical operation to relieve the obstruction is indicated Often patients* with chronic pancreatitis are much improved after removal of a chronically inflamed gall bladder After an attack of pancreatitis, patients should be forbidden the use of alcohol

For multiple *pancreatic calculi* there is no specific treatment other than the measures just outlined for chronic pancreatitis

Fibrocystic Disease

Cystic fibrosis of the pancreas a congenital and familial disease charac-

peated transfusions of whole blood may be needed, however, for best results

For improvement in the gastro-intestinal function folic acid, 10 to 20 mg daily in divided doses orally or parenterally, is most useful Calcium, either in the form of calcium lactate or calcium gluconate, 1 0 gm 3 times a day, should be given for the associated rickets in infancy and for the associated osteoporosis in adults

For the acidosis, which sometimes occurs, the patient should be given adequate parenteral fluids in the form of 5 per cent glucose in distilled water or in normal saline solution supplemented by sixth molar sodium r-lactate solution

Pancreatic Cysts

The treatment of a pancreatic cyst is surgical, with marsupialization and establishment of drainage until the amount of secretion diminishes to the point where sclerosing solutions can be applied to stop the activity of the lining cells If a fistula occurs, a secondary operation may become necessary Internal drainage may be done with the Roux Y principle

Tumors

The tumors of the pancreas considered here are carcinomata of the head, body, and tail of the organ Adenomata are considered elsewhere under Hyperinsulinism

In most instances the treatment of carcinoma of the pancreas is symptomatic This requires a diet that is easily digestible unless the patient has no symptoms, in which case he may be given a normal diet An adequate vitamin intake and fluid and electrolyte balance should be maintained When jaundice is present, a surgical anastomosis should be made between the gall bladder and stomach or gall bladder and intestines to give relief Codeine sulfate, 30 mg , or meperidine (Demerol) hydrochloride, 50 to 100 mg , or morphine sulfate, 8 to 15 mg , as the case may require, should be given freely for the relief of pain

Of recent interest, confined to the hands of surgeons experienced in this field, is radical operation with total pancreatectomy or pancreaticoduodenectomy, done preferably as a one-stage procedure The lower

cooked or raw vegetables and fruits Supplements Pancreatin 1 5 gm (one teaspoonful) per meal, oleum percomorphum, 15 drops three times a day, ascorbic acid 50 mg vitamin B complex

Therapy with the antibiotics is indicated for associated respiratory infection Staphylococcus aureus is the common offending organism and the infection should be treated with 75,000 units of procaine penicillin in aqueous solution 2 times a day for children under 1 year, 100 000 units 2 times a day for children aged 1 to 4 years, and 150,000 to 200 000 units for those over 5 years If the organism is resistant to penicillin, erythromycin 6 to 8 mg per kilogram orally 4 times a day is usually helpful Tetracycline by mouth in a dose of 25 mg per kilogram of body weight divided in 4 doses and given every 6 hours although usually less effective and frequently causing diarrhea and rectal irritation may be tried if penicillin or erythromycin cannot be used or are ineffective Without overt clinical evidence of infection triple sulfonamides 0 5 gm twice a day or sulfisoxazol (Gantrisin) in the same dosage should be used as a prophylactic measure

Celiac Syndrome

The celiac syndrome is a symptom complex in which pancreatic insufficiency is an inconstant and relatively uncommon feature In this respect as well as in the fact that it occurs in adults as non tropical sprue it differs from the fibrocystic disease of the pancreas described in the preceding paragraphs At the same time there is failure to absorb fats and vitamins and this leads to vitamin deficiencies and anemia against which treatment must be directed The *fundamental treatment for* celiac disease is dietary Every effort should be made to improve the nutrition by giving a high calorie high vitamin diet supplemented with vitamins A B C and D for a sufficiently long time Such items in the diet as protein milk banana powder fruit juices cottage cheese pureed vegetables scraped meat cooked cereals and potatoes have proved to be particularly useful in therapy In effect the diet should be high in protein moderate in fat and low in carbohydrate Intramuscular injections of concentrated liver extract, 2 0 cc (15 units) daily, and iron in the form of ferrous sulfate or ferrous gluconate 0 3 to 0 6 gm 3 times a day are indicated in improving the anemia This treatment should be supplemented with vitamin B_{12} 15 to 30 micrograms per week Re

CHAPTER XLIII

DISEASES OF THE PERITONEUM, MESENTERY, AND OMENTUM

Peritonitis

Generalized acute peritonitis should be treated with penicillin, 50,000 units intramuscularly at 2 hour intervals, combined with streptomycin, 1 to 2 gm daily or aureomycin, 500 mg in 1000 cc of 5 per cent glucose or saline every 12 hours If organisms resistant to these antibiotics are found in the peritoneal exudate an antibiotic effective against them should be used intravenously in large doses A surgeon should be consulted at once The patient should be given absolute rest propped up in bed in a sitting position Nothing should be given by mouth Fluids to correct dehydration must be given parenterally in adequate amounts, normal saline solution with 5 per cent glucose should be used No laxatives should be given If there is abdominal distention it should be relieved by Wagensteen suction or by rectal tube often both measures will be needed to relieve the distention, since both small and large intestines become filled with gas Surgery will often be necessary to remove the cause and to afford better peritoneal drainage

Localized Peritonitis The same general plan of treatment should be followed for localized inflammations of the peritoneum Collected pus should be evacuated Often an offending appendix gall bladder, or Fallopian tube will need to be removed A liver or renal abscess may be present needing to be drained Peritonitis generalized or localized is a surgical, not medical, condition, and treatment should be placed in the hands of a competent surgeon as soon as the physician suspects its existence

Chronic Peritonitis It is a striking fact that both localized and diffuse adhesive peritonitis may be present, often without causing symptoms or disturbing the motor function of the gastro intestinal tract, adhesions

fourth of the stomach, head of the pancreas, entire duodenum and the first few centimeters of jejunum should be removed Continuity is re established by gastrojejunostomy choledocho cholecystojejunostomy and entero enterostomy The neck of the pancreas should be tied off and its remains occluded It seems to be generally agreed that chole dochojejunostomy with or without cholecystojejunostomy is preferable to cholecystogastrostomy or cholecystojejunostomy because the ligated common duct may open with the escape of bile causing bile peritonitis If a total pancreatectomy is performed the patient has then been ren dered diabetic with the interesting phenomenon that he will require only 20 to 40 units of insulin daily for control of the glycosuria

BIBLIOGRAPHY

1 AYERS W B STOWENS D and OCHSNER A Fibrocystic Disease of the Pancreas *Jour Amer Med Assoc* 1951 CXLII p 7
ANDERSEN D H Cystic Fibrosis of the Pancreas in Brennenman *J Practice of Pediatrics* 1949 Vol 1 chapter 29A
3 BRUNSCHWIG A Results of Pancreatoduodenectomy *Cancer* 1949 II p 763
4 CATTELL R B and WARREN K W Pancreatic Surgery *N E J Med*, 1951 CCXLIV pp 941 975
5 HAAS S V and HAAS M P *Management of Celiac Disease* J P Lippincott, 1951
6 PETERS B J LUBITZ J M and LINDERT M C F Diffuse Calcification of the Pancreas *Arch Int Med* 1951 LXXXVII p 391
7 SHINGLETON W W and ANLYAN W G Methantheline (Ban thine) Bromide in Acute Pancreatitis *Jour Amer Med Assoc* 1951 CXLVII p 1655
8 WILLIAMS R D Chronic Pancreatitis *Am J Med* 1949 VII p 137
9 BERK J E Management of Acute Pancreatitis *Jour Amer Med Assoc*, 1953 CLII 1
10 ZOLLINGER, R M KEITH L M Jr and ELLISON E H Pan creatitis *N E J Med* 1954 CCLI 497

portal obstruction With either type the superior mesenteric vessels are involved most frequently Although the diagnosis can be suspected the true nature and extent of the process requires surgical exploration with removal of damaged intestines and anastomosis, if that is possible A careful appraisal of the patient's condition should be made with proper treatment of shock by blood transfusions, correction of fluid and electrolyte balance by giving parenterally 5 per cent glucose in normal saline solution, and by proper analgesics for pain including morphine sulfate, 8 to 15 mg, before surgery is undertaken After the operation further transfusions may be required, with specific therapy directed toward any complicating peritonitis that may be present For this purpose aureomycin 500 mg in 250 cc of saline, given intravenously every 12 hours for 5 to 7 days, is advised Penicillin, 50,000 units intramuscularly, should be given every 2 hours If infection does not respond promptly, streptomycin, 1 to 2 gm intramuscularly daily, should also be given

Disorders of the Chyle Vessels

There is no therapy available for angiomatous conditions of the chyle vessels Chyle cysts particularly if large and causing ascites or mechanical effects should be removed surgically

Mesenteric Tumors and Cysts

The treatment for tumors and cysts of the mesentery is necessarily surgical Cysts may be treated by marsupialization and tumors by direct excision

Diseases of the Omentum

Patients with abscess or inflammation of the omentum should be treated vigorously with penicillin streptomycin chloromycetin or aureomycin, singly or in combination depending on the susceptibility of the infecting organism If good response is not speedily apparent, surgical drainage is indicated

about the gall bladder or in the pelvis are very often equally symptom less, these types of chronic peritonitis need no treatment If adhesions do cause disturbance of motor function of the intestine to the degree of partial obstruction surgical exploration with possible removal of adhesions is indicated but this is not often necessary If there is no obstruction chronic peritonitis does not cause abdominal pain or constipation and another diagnosis must be sought for them Surgical exploration in the belief that pain and constipation are due to chronic peritonitis is very likely to leave the patient worse off even if chronic peritonitis with adhesions is found and corrected

Tuberculous Peritonitis This form of peritonitis should be managed by the general measures described for tuberculosis with the addition of heliotherapy with either the sun or a special lamp

Tumors of the Peritoneum

These require surgical exploration with the possibility of their removal Unfortunately they are all too often malignant with wide distribution over the peritoneal surfaces or are metastatic either into or out from the peritoneum depending on their origin For these there is no effective treatment only palliation is possible with the prevention of pain so far as is possible by the use of analgesics cordotomy or lobotomy

Mesenteric Thrombosis and Embolism

Emboli arising usually from mural thrombi in the heart are as a rule localized and unless there is occlusion of a large vessel the resulting infarction of the wall of the intestine is slight or negligible and requires no treatment If the presence of gangrene of the intestine is established however surgical operation with removal of the damaged segment of gut is necessary

Mesenteric thrombosis is a serious vascular catastrophe which if at all extensive almost invariably leads to death It may be arterial venous or both Arterial thrombosis most commonly follows local arterio sclerosis and heart disease with congestive failure Venous thrombosis is caused most commonly by intra abdominal infection neoplasm or by

Cysts infarction torsion tumors and bands of the omentum should be removed surgically as soon as the diagnosis is made Delay may lead to severe damage Pre and post operative chemotherapy with antibiotics is indicated

BIBLIOGRAPHY

Diseases of the Mesentery

1 JOHNSON C C and BAGENSTOSS A H Mesenteric Vascular Occlusion I Study of 90 Cases of Occlusion of Veins *Proc Staff Meet Mayo Clinic* 1949 xxiv p 6 8

2 JOHNSON C C and BAGENSTOSS A H Mesenteric Occlusion II Study of 60 Cases of Occlusion of Arteries and 1 Cases of Occlusion of Both Arteries and Veins *Proc Staff Meet Mayo Clinic* 1949 xxiv p 649

3 SEYBOLD W D and MUSGROVE J E Surgical Aspects of Mesenteric Vascular Occlusion *Proc Staff Meet Mayo Clinic* 1950 xxv p 585

Warm packs or an ice bag or collar, according to the patient's desires, are worth trying and often prove helpful

Diet in the beginning of the acute phase should be liquid in the form of soups, broths, fruit juices cocoa, tea, and coffee As convalescence begins, a gradual shift to bland semi solid and then a solid diet should be made with the avoidance of condiments and highly spiced foods

Chemotherapy should be employed if the infection is caused by a specifically sensitive organism Usually penicillin, 300 000 units daily intramuscularly is effective since most of the etiological organisms are sensitive to penicillin Local application of chemotherapeutic agents may increase irritation and should usually be avoided

Antihistaminic drugs such as diphenhydramine (Benadryl) hydrochloride or tripelennamine (Pyribenzamine) hydrochloride, 50 mg should be given by mouth in cases where there is an associated allergy Occasionally these drugs will prove most helpful in controlling irritation and cough in these patients They are, however, capable of causing dryness of the mouth and throat, which can be a source of irritation in some patients

Severe acute cases with obstruction of the larynx may require tracheotomy

Chronic Laryngitis

Careful search should be made for the causative factor or factors of this condition If there is nasal stenosis sinusitis, tonsillar disease, allergy or other conditions interfering with proper respiration, these should be corrected Adequate mental and physical rest is indicated Efforts should be made to maintain a high state of nutrition including adequate vitamin intake Dietary abuses such as overabundance of sweets highly spiced foods excessively hot foods, alcohol, and excessive food intake should be avoided

Coryza, tonsillitis pharyngitis acute laryngitis and sinusitis attacks should be treated promptly and thoroughly, with great care to avoid further irritation to the larynx during these attacks Absolute bed rest and vocal rest are most desirable in conjunction with the treatment recommended for the infection

Dust smoking irritating fumes and dry or too cold air should be avoided and the larynx should be rested as much as possible by a limited use of the voice Avoiding vocal abuse is essential Patients should

PART XIV

DISEASES OF THE RESPIRATORY SYSTEM

CHAPTER XLIV

DISEASES OF THE LARYNX

Acute Laryngitis

General treatment consists of laryngeal rest and the avoidance of *irritating dusts smoke dry air and air that is too cold* *Smoking should* be discontinued Severe cases should receive bed rest during the most acute phase The room should be maintained at an even temperature and should not be too cold usually 70 to 75 F is satisfactory The air should have a high humidity An electric steam generator or electrical humidifier will supply the needed moisture The stream of vapor from the steam vaporizer can be directed toward the patient's head thus insuring the inhalation of a high degree of warm moist air The addition of tincture of benzoin eucalyptus oil or menthol to the water in the generator and direct inhalation of the resulting vapor 3 or 4 times a day is soothing and pleasant A teaspoonful of the tincture of benzoin or a few drops of eucalyptus oil or menthol to a quart of water suffices Fluid intake should be generous enough to insure a urinary output of from 1500 to 2000 cc daily Severe painful non productive cough may be relieved by codeine phosphate 15 mg every 3 or 4 hours or dihydrocodeinone (Hycodan) bitartrate 5 mg 3 or 4 times a day

Acetylsalicylic acid 0 3 to 1 0 gm 2 or 3 times a day gives considerable relief of pain in many cases A combination of acetylsalicylic acid with acetophenetidin and caffeine enhances its effect Dover's powder 0 3 gm 2 or 3 times a day is often helpful in patients with cough pain and some depression

Laryngo-tracheo Bronchitis

The patient should be placed on complete bed rest in a room where the air is humid and warm, and he should be observed closely for signs of respiratory impairment, the attending physician should be prepared to perform a tracheotomy on short notice if respiration becomes of the obstructive type Fluid intake should be liberal Diet should be liquid with the avoidance of hot or spiced foods

If obstruction occurs aspiration of secretions and viscid obstructing exudates by suction tube or bronchoscopic drainage is essential If obstruction is not relieved, tracheotomy is indicated at once

Chemotherapy should be given promptly, usually penicillin is the most effective As soon as the organism is known, treatment should be directed specifically against it by the use of the most effective antibiotic

The possibility of diphtheria must be considered, and throat cultures made at once When in doubt, 20 000 units of diphtheria antitoxin should be given while the physician is waiting for definite diagnosis by culture If *Hemophilus influenzae* is the causative organism streptomycin or concentrated rabbit antiserum, as described for Influenzal Meningitis should be given Unfortunately the frequent presence of this organism in throat cultures of persons not ill renders its recognition as the causative organism difficult

If cardiac failure develops, it should be treated promptly

Transfusion of blood is of definite benefit if there is moderate anemia Atropine sulfate meperidine (Demerol) hydrochloride, and the opiates should be avoided as should heavy sedation, since they dry the secretions and dull the cough reflex

Spasmodic Laryngitis Laryngismus Stridulus Croup

The treatment for this alarming but not dangerous condition which occurs most commonly in young children between the ages of 2 and 6 consists in relief of the immediate attack followed by measures to prevent recurrence The acute attack although presenting the most frightening symptoms usually responds readily to therapy The child should be reassured by the parents, who by calm, soothing care can quiet his fears The parents should be cautioned against showing any alarm over the situation since any fear shown by them will frighten the child

communicate with pencil and pad as far as possible Oral hygiene should be strict Diseases of the gums and teeth should receive careful attention Chronically inflamed tonsils should be removed

If there is trickling of pharyngeal secretion into the larynx during sleep, the patient should sleep with the head turned to one side rather than on the back and not more than one pillow should be used unless this causes respiratory discomfort

Steam inhalations with tincture of benzoin eucalyptus oil or menthol added to the water as described under Acute Laryngitis are soothing and may be given before retiring

The local application of silver nitrate solution or other irritating agents is not advised

Residence near the seashore is beneficial to many if the climate there is not too variable Dusty dry climates are to be avoided

Edematous Laryngitis

If no dyspnea is present treatment may be along conservative lines with the physician on the alert to detect any progression

Ice bag to the larynx moist warm air in the room vocal rest bed rest with the head elevated and avoidance of irritating dusts smoke or fumes are helpful general measures Treatment should be directed toward the causative factor Infections susceptible to chemotherapy should be treated by the proper agent If there is renal or cardiac failure appropriate treatment should be given

If the causative factor is angioneurotic edema epinephrine hydrochloride 1 1000 solution 0 3 to 0 6 cc is to be given intramuscularly *every hour until the condition is relieved or toxic signs appear* Antihistaminic drugs by mouth such as diphenhydramine (Benadryl) hydrochloride or tripelennamine (Pyribenzamine) hydrochloride 50 to 100 mg at 3 or 4 hour intervals are helpful A local spray of 1 100 epinephrine hydrochloride solution may be necessary in an occasional case

Patients with dyspnea should be under careful observation so that a tracheotomy may be performed if obstruction is not relieved by expectant treatment *Tracheotomy is safer and to be preferred to intubation* Delay in performing it is responsible for much of the high mortality in these cases

CHAPTER XLV

DISEASES OF THE BRONCHI

Acute Tracheitis Tracheobronchitis Bronchitis Bronchiolitis

Infections of the lower respiratory tract are most commonly caused by such bacteria as streptococci, staphylococci, diphtheria bacilli, pneumococci, and, occasionally, a virus A specimen of expectorated secretion should be carefully collected at once with proper smears and cultures made to identify the causative agent, but sometimes no etiological factor can be determined If the etiological agent is found, the proper antibiotic should then be chosen and given in appropriate doses Further measures should be symptomatic for relief of pain, rawness, and distressing cough

The patient should be put to bed and given a nutritious diet with adequate fluid intake

Since streptococci, staphylococci, and, occasionally, pneumococci cause by far the majority of such infections, it is best to begin treatment with penicillin Procaine penicillin in aqueous suspension 300,000 units fortified with 100,000 units of soluble penicillin, should be given intramuscularly twice a day In the event that cultures subsequently demonstrate organisms resistant to penicillin or better controlled by other antibiotics, change should be made to aureomycin, streptomycin, chloramphenicol, or terramycin as indicated In case diphtheria is suspected or demonstrated, antitoxin therapy should be instituted immediately

During the day the patient should be encouraged to expectorate secretions, this may be helped by the administration of 10 to 15 drops of saturated solution of potassium iodide, 3 times a day in water or milk Syrup of hydriodic acid U S P, 4 cc 3 times a day, is palatable and effective but is a more expensive preparation Heavy sedation and measures to suppress cough during the day should be avoided Cough mixtures

further The air in the room should be warm humid and free from irritating smoke dust or fumes Steam inhalation should be started promptly Inhalation of amyl nitrite may give prompt relief A dash of cold water on the face is occasionally helpful Syrup of ipecac 2 to 4 cc should be given The ipecac should induce vomiting If it does not the dose may be repeated once or possibly twice at intervals of 20 or 30 minutes to insure vomiting After all nausea has subsided a mild sedative such as phenobarbital 15 to 30 mg may be given If the required apparatus is at hand during an acute attack direct oxygen insufflation by means of the laryngoscope will give excellent results

In view of the tendency toward recurrence means should be available to handle subsequent attacks The general hygiene and nutrition of the child should be improved and brought up to a high level Vitamin D and calcium intake should be high Nervous tense excitable children who exhibit this syndrome should receive additional rest Chronic upper respiratory infections should receive careful attention and every effort should be made to avoid irritation of the respiratory tract Cold air may be very irritating to the mucous membranes during upper respiratory infections and may precipitate attacks in susceptible cases

After an attack measures should be taken to prevent recurrences The child should sleep in a room where the air is warm (70 F) and well humidified *At bedtime a subvomiting dose of syrup of ipecac 0 5 to 1* cc and a sedative dose of phenobarbital 15 to 30 mg should be given for the following or 3 evenings If hoarseness develops during the day or a cough appears in a child subject to these attacks the preventive measures given above should be employed

Intubation and tracheotomy are not indicated

tory organisms can be combatted successfully with 300,000 units of procaine penicillin in aqueous suspension fortified with 100,000 units of soluble penicillin given intramuscularly once or twice a day For organisms not sensitive to penicillin, aureomycin or terramycin in the usual doses should be given Tuberculous bronchitis (tracheo-bronchial tuberculosis) should receive the treatment recommended in the section on Tuberculosis

More and more bronchoscopic examination is demonstrating its usefulness in diagnosis of the cause of various types of chronic bronchitis in treatment by aspiration of thick, tenaceous secretions, in the removal of polyps and in the diagnostic instillation of iodized oil, which also may frequently be soothing to the bronchial mucosa for extended periods of time

Treatment consists of measures that give symptomatic relief, eliminate infection and abnormal secretions from the bronchial passages, and regulate the type of respiration and general activities of the patient Obesity should be corrected promptly and all sources of infections such as teeth sinuses and tonsils, should be cleared Acute respiratory infections should be given prompt and adequate treatment to prevent complications or more serious infections Moderate exercise in the morning with deep breathing is helpful The abdomen should be contracted from below upward with a series of forceful respirations For some patients a controlled cough at the end of expiration will aid in removing irritating secretions However, these exercises must not be carried out to the extent of causing fatigue tachycardia, or other signs of overexertion In some patients who have bronchial spasm emphysema and fibrosis the use of bronchodilator drugs and intermittent positive pressure breathing is most helpful in restoring the lung to better functioning ability, removing irritating secretions and giving the patient much subjective improvement This has been brought out very clearly in the work of Gordon and Motley The procedure consists of giving the patient an aerosol suspended in 100 per cent oxygen containing cetylpyridinium (Ceepryn) chloride 3 drops of a 1 1000 solution, as a wetting agent and either phenylephrine (Neosynephrine) hydrochloride 8 drops of a 1 per cent solution diluted in 1 cc of physiological saline, or racemic ephinephrine (Vaponefrin), 8 to 16 drops of a 1 per cent solution in 1 cc of physiological saline by means of a respirator The respirator should have a pressure or flow sensitive valve face mask and necessary regulators to permit the introduction of 100

should be used particularly at night to insure proper rest Most effective are those containing codeine phosphate 15 mg per dose as prescribed below if desired dihydrocodeinone (Hycodan) bitartrate may be substituted for the codeine so that the dose given contains 5 mg of the drug

Rx	Codeine phosphate	0 2 gm
	Ammonium chloride	25 0 gm
	Syrup of citric acid	50 0 cc
	Water to make	100 0 cc
Sig	Take 2 teaspoonfuls every 4 hours	

For tracheal distress and rawness proper humidification of the air is very effective the air of the room should be kept warm and saturated with moisture Steam inhalations or 3 times a day are soothing and to these may be added compound tincture of benzoin or oil of eucalyptus *1 teaspoonful to a quart of water If bronchiospasm is present* ephedrine sulfate 4 mg 2 or 3 times a day is beneficial When cyanosis is present the patient should be placed in an oxygen tent

In older individuals an attack of bronchitis can place a heavy load on the heart and circulation and cardiac failure requiring treatment may develop

Chronic Bronchitis

Chronic bronchitis is usually secondary to some other condition namely infection obstruction aneurysm mediastinal tumor hypothyroidism or cardiac failure The causative factor or factors should be sought out carefully and corrected whenever possible These causative factors may include tobacco smoke dusts bacterial infections of the sinuses nose or throat polyps in the bronchi or bronchostenosis from any cause leading to obstruction with secondary infection tuberculosis aortic or pulmonary aneurysm tumors compressing the bronchi hypothyroidism (myxedema) with its tissue changes and chronic cardiac failure with pulmonary congestion Stereoscopic roentgen ray studies of the chest are imperative for accurate diagnosis before treatment is begun

When any sputum is being raised by the chronic cough it should be examined for tubercle bacilli by smear and culture or by guinea pig inoculation if the former do not show the organism The usual respira

ing from the hips over the side of the bed with his hands on the floor, if he can manage it If the patient is very ill, elevation of the foot of the bed will be helpful, with the patient lying flat If the lesion is unilateral, the patient should lie turned on the normal healthy side to promote drainage Such postural exercises should be carried out 4 times a day, first thing in the morning, before lunch, before supper, and at bedtime They should be carried out on an empty stomach for after a full meal the procedure may cause vomiting

Various measures should be used to thin bronchial secretions and to promote expectoration Cough sedatives should be avoided during the day and should be used at night only if necessary to insure rest To thin the secretions and to promote expectorations either ammonium chloride or potassium iodide may be used Ammonium chloride is to be given preferably in 0 5 to 1 0 gm enteric-coated tablets 4 times a day Saturated solution of potassium iodide, 10 to 15 drops given 4 times a day in water or milk is usually effective If intolerance to iodides develops, either with gastric upset, salivation or skin rash, ammonium chloride should be used If the sputum is fetid, benefit may be obtained by the use of calcreose 0 3 gm given 3 or 4 times a day Excessive secretion and a moist productive cough are usually helped by terpene hydrate, which tends to be soothing to the bronchi and to dry up excessive secretion

For mild cough 30 mg of codeine phosphate by hypodermic injection is useful The cough often occurs in severe paroxysms for which such measures as dihydrocodeinone (Hycodan) bitartrate, 5 to 15 mg hypodermically, may be required Occasionally morphine sulfate is necessary in doses of 8 mg given by hypodermic injections

Every effort should be made to isolate and to identify invading organisms, including spirochetes and tubercle bacilli with the proper selection of chemotherapeutic and antibiotic agents to combat them With the organisms usually found to be present in bronchiectasis penicillin should be employed It should be administered both locally and parenterally Since penicillin is not without irritating effect when applied to the mucosa in some individuals and is much less effective in this form than adequate parenteral penicillin the use of the finely particled aerosol is not advised as an inhalation therapy Intramuscular administration of procaine penicillin in aqueous suspension 300 000 units plus 100 000 units of soluble penicillin, twice a day is usually sufficient For bronchial spirochetosis penicillin is also advised If penicillin resistant

per cent oxygen These intermittent positive pressure aerosol oxygen administrations should be given for 15 to 20 minutes 2 or 3 times a day and may be continued for from 4 to 6 weeks or longer if the need is indicated by the condition of the patient Diaphragmatic elevation with an abdominal support that produces abdominal compression and so displaces the diaphragm to a higher level helps provide a more effective respiration Usually very little can be gained by the use of expectorants or cough depressant drugs Codeine should not be used unless there is such severe coughing as to cause great discomfort and possibly increase lung damage since its use actually leads to retention of secretions and perhaps more bronchiolar spasm Potassium iodide or ammonium chloride as recommended for bronchiectasis may be given a trial and occasionally will thin secretions and loosen tenacious mucus Usually however results from their use are disappointing

Of greatest importance is the recognition of chronic low grade congestive cardiac failure Cough is a common symptom of cardiac failure and may be considered erroneously to be due to chronic bronchitis however the two may co exist Treatment of the cardiac decompensation with bed rest digitalis and diuretics as outlined under Heart Failure often gives most gratifying results in such patients

Since chronic bronchitis occurs so commonly in older people and is frequently aggravated by change of climate to cold damp weather residence in an equable climate is very useful Repeated respiratory infections should be avoided and when contracted, should be treated thoroughly with bed rest fluids and properly chosen antibiotic therapy if organisms sensitive to chemotherapy can be isolated

Bronchiectasis

Bronchiectasis may be seen in childhood and at this age may be a congenital anomaly the more common form is seen in adult life Both types are usually infected secondarily Roentgenograms following iodized oil (Lipiodol) installation are necessary for diagnosis Tumor or stenosis proximal to the area of bronchiectasis should be looked for diligently and removed if possible Management of this condition may be considered under medical and surgical treatment

Medical Treatment This should consist of measures to rid the bronchi of the thick tenaceous secretions and to eliminate infection Postural drainage is most effective carried out preferably by the patient s hang-

otherwise healthy individuals, who are good surgical risks, lobectomy or pneumonectomy as indicated should be advised In skilled hands the operative mortality from pneumonectomy today is no greater than for any major surgical procedure, and the results are apt to be so satisfactory that they justify the operative risk If it is to be undertaken its use should not be delayed Rapidly it is becoming the treatment of choice

Bronchial Asthma

From the standpoint of therapy patients with asthma may be divided for convenience into two groups (1) those whose asthma is due to sensitivity to an outside source, such as dusts, pollens, foods, and so on — also called extrinsic or bronchial asthma, and (2) those with asthmatic symptoms associated with chronic bronchial infection (intrinsic asthma) — sometimes called asthmatic bronchitis

The treatment of the underlying abnormality is different in the two types In the extrinsic, sensitivity cases there is a fundamental defect in tissue responsiveness, called atopy, and tests for all kinds of offending proteins should be carried out These are best accomplished as skin tests with the protein substances of pollens, grasses, dusts, foods and animal danders in an attempt to find the offending agent or agents, so they can be eliminated as provocative substances In the case of foods and animal emanations, treatment is best carried out by simply avoiding them Desensitization to foods and emanations can be accomplished by inoculations, but it is extremely difficult to obtain good results In the case of dusts, grasses and pollens desensitization should begin with very small doses of dilute solutions, given 3 months before symptoms begin, if symptoms are seasonal The dose should be increased gradually at no less than 5-day intervals, preferably 7, to a strength not to exceed 1 500 usually this has been found to be very successful In instituting so called preseasonal treatment, dilutions should be made of the offending proteins, in strengths of 1 500, 1 1000, 1 5000 1 10,000 1 20 000 1 40 000, 1 80,000, and 1 160,000 Skin tests should be made on the forearm with each of these dilutions, then the strength of dilution with which the patient shows no reaction should be chosen as the dilution with which to start treatment If the method above is carried out each season treatment should start with the dilution then determined as the one not giving a reaction, for sensitivity may vary from year to year

organisms are found to be present or if they develop during therapy streptomycin by intramuscular injection should be given in a dose of 1 0 gm every other day Aureomycin chloramphenicol or terramycin should be given in addition to the penicillin if organisms sensitive to them indicate the need Any of these agents should be used intermittently to avoid the possible development of secondary pulmonary moniliasis

Expectoration of bloody mucus is a common symptom in bronchiectasis and the proper treatment of the bronchiectasis as already outlined will usually cause this symptom to subside Massive hemoptysis should be treated with complete bed rest reassurance and adequate sedation to allay fear and apprehension If morphine is used small doses such as 6 mg should be given hypodermically and repeated infrequently Larger doses may suppress respiration prevent cough and allow the accumulation of purulent material blood and clots with resulting pneumonia If it can be determined from which lobe the blood is coming an ice bag to that part of the chest may be useful Splinting of the involved side of the chest with sandbags is helpful If the hemorrhage is large and persistent artificial pneumothorax is advised provided pleural adhesions often present do not prevent collapse of the lung

Certain general measures are of importance in medical treatment A warm equable climate is very useful The maintenance of good nutrition is essential in decreasing acute exacerbations of infections so important in this disease The same corrective measures for upper respiratory tract infections should be carried out as discussed under Chronic Bronchitis Smoking should be prohibited

Surgical Treatment The measures outlined in the preceding paragraphs under medical treatment are essentially palliative because they have no effect on the abnormally dilated bronchi Since bronchial dilatation may be secondary (distal) to stenosis or tumor bronchoscopic examination is useful in delineating such tumor or stenosis and possibly in correcting it Bronchoscopy is also useful in removing thick tenacious secretions but it should not be performed repeatedly although some physicians do not consider this harmful Iodized oil if injected by bronchoscope or instilled through a tracheal catheter may be useful in treatment as well as in diagnosis for the soothing effect frequently given by it If the bronchiectasis is primary and localized preferably unilateral and especially if present in the younger age groups and

otherwise healthy individuals, who are good surgical risks, lobectomy or pneumonectomy as indicated should be advised In skilled hands the operative mortality from pneumonectomy today is no greater than for any major surgical procedure, and the results are apt to be so satisfactory that they justify the operative risk If it is to be undertaken its use should not be delayed Rapidly it is becoming the treatment of choice.

Bronchial Asthma

From the standpoint of therapy patients with asthma may be divided for convenience into two groups (1) those whose asthma is due to sensitivity to an outside source, such as dusts, pollens, foods, and so on — also called extrinsic or bronchial asthma, and (2) those with asthmatic symptoms associated with chronic bronchial infection (intrinsic asthma) — sometimes called asthmatic bronchitis

The treatment of the underlying abnormality is different in the two types In the extrinsic, sensitivity cases there is a fundamental defect in tissue responsiveness, called atopy, and tests for all kinds of offending proteins should be carried out These are best accomplished as skin tests with the protein substances of pollens grasses dusts foods and animal danders in an attempt to find the offending agent or agents, so they can be eliminated as provocative substances In the case of foods and animal emanations, treatment is best carried out by simply avoiding them Desensitization to foods and emanations can be accomplished by inoculations, but it is extremely difficult to obtain good results In the case of dusts grasses, and pollens desensitization should begin with very small doses of dilute solutions given 3 months before symptoms begin if symptoms are seasonal The dose should be increased gradually at no less than 5-day intervals preferably 7, to a strength not to exceed 1 500 usually this has been found to be very successful In instituting so-called preseasonal treatment, dilutions should be made of the offending proteins, in strengths of 1 500, 1 1000, 1 5000, 1 10 000, 1 20 000 1 40 000, 1 80,000, and 1 160,000 Skin tests should be made on the forearm with each of these dilutions, then the strength of dilution with which the patient shows no reaction should be chosen as the dilution with which to start treatment. If the method above is carried out each season, treatment should start with the dilution then determined as the one not giving a reaction, for sensitivity may vary from year to year,

thus serious reactions will be avoided As a general rule, if successful preseasonal treatment has been carried out over 5 consecutive years, *approximately 70 per cent of all patients will become permanently* desensitized

The antihistaminic agents are very useful in the treatment of mild or even moderate hay fever but they are practically without benefit in the treatment of bronchial asthma

In intrinsic asthma or asthmatic bronchitis the approach to treatment should be the same as outlined for Chronic Bronchitis and Bronchiectasis A vigorous attack with intermittent antibiotic therapy should be made against any infection that is present with additional measures directed toward aiding the expectoration of a thinned mucus and the control of cough

Frequently acute attacks of asthma can be treated in the home and do not require hospitalization As a home remedy stramonium leaves and potassium nitrate burned together on a plate may be very useful

Rx	Powdered stramonium leaves	1 0 gm
	Potassium nitrate	1 3 gm
Sig	Ignite small amount of powder and inhale fumes	

Some prefer inhalation of smoke from cigarettes containing stramonium leaves and potassium nitrate

Treatment of the Acute Attack of Asthma Everything that wheezes *is not asthma* *Of first importance is to rule out cardiac dyspnea* (cardiac asthma) and the presence of bronchial tumors polyps or foreign bodies with obstruction as the cause of the wheezing respirations When the asthma is due to edema of bronchial mucosa and/or bronchial spasm the treatment is the same whether it is bronchial asthma or asthmatic bronchitis Epinephrine (Adrenalin) hydrochloride by hypodermic injection is the treatment of choice Begin with an aqueous 1 1000 solution and administer doses of 0 1 to 0 3 cc for a child 0 2 to 0 3 cc for an adult repeated as often as every 20 to 30 minutes Care must be used in giving epinephrine to a patient with angina pectoris increased blood pressure however need be no deterrent for aqueous epinephrine *given in this way seems to have little effect on the blood pressure even if very high in a patient with an acute attack of bronchial* asthma

If the acute attack becomes prolonged a longer acting preparation such as epinephrine (Adrenalin) in oil 1 500 may be used subcuta-

neously at 4- to 6 hour intervals in doses of 0 25 to 0 5 cc In the very severe acute attack some prefer the use of aqueous epinephrine (Adrenalin), 1 100 dilution, by inhalation through an atomizer, but its frequent use should be avoided since it can cause damage to the nasal mucosa.

Isopropylarterenol (Isuprel) hydrochloride, best given as a 1 200 aerosol inhalation in a dose of not more than 5 cc, is helpful, but the unpleasant side reactions of tachycardia, palpitation, dizziness, and excitement limits its usefulness

Morphine should not be given, for it slows respiration, increases bronchial spasm, reduces the oxygen intake which the patient needs so vitally, and is habit-forming Meperidine (Demerol) is of limited value and is likewise not recommended A carefully chosen sedative is very useful, however, for emotional upsets can precipitate attacks of asthma in a susceptible individual, and a prolonged acute attack often leads to emotional disturbances which may establish a vicious cycle Small doses of a barbiturate or chloral hydrate are advised Phenobarbital 15 to 30 mg by mouth every 4 to 6 hours, or sodium phenobarbital, 60 mg intramuscularly every 8 hours is useful Chloral hydrate, 0 3 to 1 0 gm in iced orange juice, repeated in 6 hours, is helpful

If the patient is epinephrine fast, in an acute attack treatment should be begun with sedatives as outlined in the preceding paragraph, and aminophyllin, 0 5 gm, should be given intravenously at 1- to 2 hour intervals for perhaps 3 to 4 injections Following this, epinephrine in small doses (0 2 to 0 3 cc) should be tried, often it will be successful, for under these circumstances aminophyllin frequently has the peculiar quality of restoring epinephrine effectiveness

Potassium iodide, 1 to 3 gm by mouth daily if necessary, or sodium iodide, 1 0 to 2 0 gm intravenously daily in physiological saline solution, is helpful in loosening a thick tenaceous sputum

An oxygen tent in which 8 liters of 100 per cent oxygen are given per minute is very useful Added helium, when available, in concentration of not less than 60 per cent, is preferred by many to pure oxygen The gases should be passed through water to prevent too great a drying effect on respiratory mucosa

During the acute attack adequate fluid intake should be maintained Intravenous 5 per cent glucose solution 1000 to 2000 cc, should be given if there is dehydration A soft easily digestible diet is advised

Treatment of Status Asthmaticus Preferably the patient should be in the hospital in a quiet, dust free room Simply the change of scenery

from home to hospital accomplishes much in beginning treatment Air or foam rubber pillows and mattresses should be provided when available lest dust or feathers continue to provoke the attack

The patient should be placed in an oxygen tent with 8 to 10 liters of 100 per cent oxygen per minute or oxygen mixed with 60 per cent helium if that is available. Care must be exercised in giving oxygen which causes dryness and a thickening of the mucosa In the presence of carbon dioxide accumulation oxygen is definitely harmful Accumulation of carbon dioxide can be detected by doing a carbon dioxide serum combining power measurement if its presence is demonstrated oxygen must be withheld or used with great caution in order to avoid respiratory-center failure The accumulation of carbon dioxide causes narcosis and failure of the center while the relative lack of oxygen serves as an effective stimulus to the center If the oxygen level is raised this stimulus is lost and failure ensues

A sedative as outlined under treatment for the acute attack should be given at once If the patient is epinephrine fast as is often the case in status asthmaticus intravenous aminophyllin, 0.5 gm every hour as outlined under treatment of the acute attack should be tried

Cortisone by mouth in doses of 25 to 50 mg every 6 hours for as long as 5 to 7 days or corticotropin 20 to 40 mg subcutaneously 2 times a day have been found to be very effective in the treatment of status asthmaticus Corticotropin may also be given intravenously 15 to 25 mg in 500 to 1000 cc of 5 per cent glucose in distilled water slowly over 8 hours Improvement is not necessarily maintained however after withdrawal of therapy Withdrawal of cortisone may restore the therapeutic effectiveness of other agents, particularly epinephrine These drugs have not been sufficiently studied to determine their actual effectiveness in relation to their not infrequent highly undesirable reactions Experience already gained indicates that in many cases there may be a serious exacerbation of the asthma when they are withdrawn

Frequently by the time these patients reach the hospital most known measures have been tried without success It is of first importance to reassure the patient that he is not going to die of the attack for the outcome is rarely fatal this confidence will ease the emotional stress and aid breathing At this point it is frequently useful to stop all treatment except mild sedatives to force fluids such as water and fruit juices by mouth and to give 5 per cent dextrose in distilled water parenterally 2 to 4 liters per day since by this time the patient is usually dehydrated

A prescription that may be used with much benefit is potassium iodide, 20 0 gm , syrup of wild cherry, 120 cc , give 1 teaspoonful every 4 hours If iodides cannot be given by mouth, an intravenous infusion of 1000 cc of 5 per cent dextrose containing 1 0 gm of sodium iodide should be given Ammonium chloride, 20 0 gm , in syrup of wild cherry, 120 0 cc , given in a dose of 1 teaspoonful every 4 hours is also helpful and can be used if iodides have caused a reaction or are undesirable for any other reason In children with status asthmaticus, 1 to 2 teaspoonfuls of syrup of ipecac to produce emesis may be helpful The adult dose is 3 or 4 teaspoonfuls

If the attack should continue unabated, resort may be had to the rectal administration of ether and oil, 30 to 60 cc per 40 pounds of body weight Bronchoscopy may be carried out to remove any inspissated mucus or plugs If the patient is unconscious a respirator may be necessary, but its use requires great care to prevent forcing mucus down into the smaller bronchi The air in the room must have a high humidity and steam inhalations may be given to ease irritation

In severe bronchial asthma and status asthmaticus in which all methods of medical management have failed, some success has been claimed for bilateral resection of the posterior pulmonary plexus In such circumstances, this operation may be tried

After return of epinephrine responsiveness, periodic injections of epinephrine should obviously be instituted as described under treatment for the acute attack

When the attack has subsided the patient should remain in bed for several days and be given adequate fluids and a nourishing diet, then ephedrine sulfate 24 mg 2 or 3 times a day should be given by mouth For those made excitable by ephedrine combinations of ephedrine amytal or ephedrine pentabarbital (Nembutal) in similar dosage may be used Such combinations are particularly useful for bedtime administration in those who have nocturnal attacks of bronchial asthma

Interval (Preventive) Treatment Measures should be instituted as already outlined under Bronchial Asthma and Asthmatic Bronchitis Continued expectoration of secretions so they will not accumulate is to be encouraged by the use of saturated solution of potassium iodide 10 to 15 drops 3 or 4 times a day taken in water or milk At the same time it is useful to prescribe ephedrine sulfate in 24 mg doses 3 or 4 times a day alone or combined with theophylline and phenobarbital as Luasmin or Tedral Sunshine fresh air, an equitable climate, avoidance

of infection and fatigue and reduction of weight in the obese patient should be prescribed in an attempt to prevent further attacks Psycho therapy is important during this period

TUMORS

The tumors of the bronchi to be considered in this section are benign tumors (adenomata, polyps) adenocarcinomata and other malignant tumors Other tumors arising in the lungs cystic disease dermoid cysts and metastatic tumors are considered under Diseases of the Lungs Tumors of lymph nodes are considered under Diseases of Lymph Nodes

The principle benign tumors of the bronchi include simple adenomata arising from the mucous membrane chondromata arising from bronchial cartilage and occasionally lipomata Benign in themselves they may cause much disturbance in the form of chronic cough inspiratory or expiratory obstruction (asthma) hemoptysis and with narrowing of air passages bronchiectasis suppuration and gangrene of the lungs Polyps particularly on a pedicle can produce a ball valve action resulting in recurrent attacks of pneumonitis Only by their size or particular position do they cause such manifestations Under such circumstances they should be looked for diligently and removed through a broncho scope

The most important primary tumor of the bronchus is the adenocarcinoma Its incidence is increasing and the mortality is still extremely high Some believe that the increase in tobacco smoking is an im portant factor in etiology and in the increased incidence If this is true it is important in any attempt to prevent the disease

The treatment of bronchogenic carcinoma should be early radical excision of the tumor It cannot be emphasized too strongly with adeno carcinoma of the bronchus that if successful excision is to be carried out it must be done at the earliest possible moment All too often by the time the roentgenographic evidence is certain the tumor is already beyond cure in most cases Nevertheless with cough parti cularly paroxysmal pain in the chest and/or hemoptysis this condition should be suspected and the diagnosis by x ray should be made promptly then lobectomy or pneumonectomy should be carried out In skilled hands the immediate operative mortality is relatively low at the present time

Foreign Bodies

It is important to remember the possibility of a foreign body in the bronchus, particularly in children, in the differential diagnosis of all forms of lung disease The manifestations of a bronchial foreign body are extremely variable, including cough, evidence of inflammation wheezing and the x ray demonstration of atalectasis, pneumonitis, bronchiectasis, and suppuration On the other hand there may be no symptoms whatever The type of material, size, and location of the foreign body determine the symptoms Not all foreign bodies are radio-opaque nuts and peanuts are classic examples

The definitive treatment should consist in the removal of the foreign body by the bronchoscope Do not wait for the spontaneous coughing out of a foreign body, from this, laryngeal impaction or subepiglottic edema may occur requiring tracheotomy If there is secondary infection adjacent or distal to the foreign body, it should be treated with antibiotics, depending on the organism which has been isolated Penicillin is likely to be the effective antibiotic and should be given intramuscularly 300,000 units twice a day

CHAPTER XLVI

DISEASES OF THE LUNG

Chronic Passive Congestion and Edema

Usually both of these conditions are the result of cardiac insufficiency as a part of cardiac decompensation. Of prime importance is the application of treatment described under Chronic Cardiac Decompensation. For *acute edema of the lungs* in addition to the use of a digitalis preparation and a mercurial diuretic, venesection with removal of 200 to 500 cc of venous blood should be performed and the patient given a hypodermic of 8 mg. of morphine sulfate and 0.5 to 1.0 mg. of atropine sulfate. As a rule these last 2 measures relieve the acute pulmonary edema quickly, while continuing adequate treatment of the underlying cardiac condition will prevent its recurrence or render an attack, if it does occur, less severe. Some patients with chronic cardiac decompensation develop acute pulmonary edema when put to bed, while they remain free if permitted to sit propped comfortably in a chair over a period of a few days of carrying out a more effective regime of treatment of chronic cardiac insufficiency.

Paroxysmal Dyspnea. When not caused by bronchial asthma, this is due to a type of cardiac decompensation and is especially common in patients with hypertension. It may occur often in nocturnal form in patients in whom this is almost the only evidence of cardiac decompensation. It must be distinguished from bronchial asthma, the treatment of which would be very different. The treatment of paroxysmal dyspnea should be that described for acute pulmonary edema. A rectal suppository of aminophyllin 0.5 gm. every 4 or 6 hours or at bedtime for nocturnal attacks is most effective for paroxysmal dyspnea.

Hemoptysis

Whatever its cause, any considerable hemoptysis is to be treated by immediate bed rest and reassurance. To cough up blood is very fright

ening to patients, but only very rarely is it of serious consequence The patient who has had a previous hemoptysis knows that and knows what to do, so often he merely goes to bed and may not even call for his physician to come The accompanying cough, which is usual, should be controlled by a hypodermic of 30 mg of codeine phosphate, if this is not effective a hypodermic of 15 mg of morphine sulfate with 0 5 mg of atropine sulfate should be given If hemoptysis continues the most effective measure to use is an artificial pneumothorax After the hemoptysis ends the anemia should receive repeated small transfusions of blood, 200 cc each time is a desirable amount, since larger amounts of blood may start renewed hemoptyses

Pulmonary Fibrosis Including Pneumonoconiosis and Silicosis

Prevention is more important than treatment Methods of prevention should be instituted, even if the pulmonary process has started, and the sooner that this is done the better Prevention should consist of protection against the entrance into the lung of the agent or agents known to be possibly causative or which already have begun to produce lung damage Infectious diseases such as pneumonia, tuberculosis syphilis, and various mycoses which pulmonary fibrosis may accompany, should be treated as described under these several headings Active measures to overcome bronchial spasm and bronchiolitis should be carried out as recommended by Gordon and Motley These consist of graded exercises and deep breathing exercises especially holding the abdomen from below upward during a series of forceful expirations The use of intermittent positive pressure breathing with a respirator may be tried Oxygen, 100 per cent should be given while simultaneously administering an aerosol containing a wetting agent, cetylpyridinium (Ceepryn) chloride 3 drops of a 1 1000 solution, and phenylephrine (Neosynephrine) hydrochloride or racemic epinephrine (Vaponefrin), 8 drops diluted with an equal amount of isotonic sodium chloride These positive pressure breathing treatments should be given for 15 to 20 minutes 2 or 3 times a day depending on the condition of the patient If fatigue, palpation or tachycardia develops the time and dosage of the drugs should be reduced This treatment, combined with interval exercises and diaphragmatic elevation by suitable abdominal support to facilitate bronchial drainage leads to expectoration of large amounts

of irritating material and gives considerable relief from the asthma like attacks Bronchiectasis with its attendant fibrosis should be treated as described under that heading For silicosis aluminum by the inhalation or insufflation of grease free aluminum in very finely powdered form has been widely used Its permanent value is doubtful Subjectively the patients feel better but there is no objective evidence of improvement

Cough so often a very uncomfortable sequence to pulmonary fibrosis results from the accompanying bronchiospasm bronchitis and chronic infection of the bronchi The latter element should be treated with penicillin or other antibiotic found to be effective against the bacteria isolated from the sputum Various sedative cough mixtures as described under Chronic Bronchitis should be used but sedative cough mixtures should be used only to control severe racking cough They can be harmful since sedation leads to retention of secretions

Mechanical aerations of the pulmonary tract of various sorts have been *found helpful largely by relieving areas of atelectasis that form Various* breathing exercises and abdominal supports also help Moving to a dust less equitable climate is desirable for many of these patients if it is economically possible

Corticotropin 25 to 75 mg intramuscularly daily or cortisone 100 *to 200 mg orally or intramuscularly frequently gives excellent help and* enables the patient to remain comfortable for long periods of time

EMPHYSEMA

Bronchitis frequently accompanies emphysema of the lungs it should be treated as described under Acute and Chronic Bronchitis Penicillin procaine in aqueous suspension 300 000 to 600 000 units intramuscularly daily is usually effective in clearing bronchial infection For some or*ganisms streptomycin 2 0 gm every other day will be effective when* penicillin is not When both of these fail aureomycin or terramycin depending on the sensitivity of the organism should be used in the usual dosage In some of these patients there is present some degree of cardiac insufficiency test for this should be made and if they show the *existence of cardiac insufficiency* digitalis therapy should be given

When dyspnea is urgent oxygen inhalation is indicated With cyanosis and distended neck veins bleeding with removal of 500 cc of blood is needed In adults abdominal pressure by a special binder or corset to

elevate the diaphragm will aid breathing In many of these patients there is an element of asthma, so-called asthmatic emphysema, in these 0 2 to 0 3 cc of a 1 1000 epinephrine (Adrenalin) hydrochloride solution given hypodermically, along with other therapy described in the section on Bronchial Asthma, will give much relief For longer action, ephedrine sulfate, 24 mg or ephedrine and pentobarbital capsules, containing 24 mg each of ephedrine hydrochloride and pentobarbital (Nembutal), 1 or 2 capsules every 4 to 6 hours, may be very effective Surgery on the ribs has given some evidence of effectiveness and might be considered for very stubborn cases Breathing exercises are desirable procedures In miner's emphysema, oxygen under positive pressure has been found to be very useful Many of these patients, especially older ones, are much worse in the winter than in the summer They have so called chronic winter colds For these, residence during the winter in a warm, non-dusty climate is highly desirable

Gangrene and Abscess

For these conditions immediate intramuscular treatment with 100,000 units of penicillin should be begun the dosage being repeated every 3 hours so long as fever continues If response is not satisfactory, dosage should be doubled As soon as possible the causative organism should be diagnosed by bacteriological methods and its sensitivity to penicillin and other antibiotics determined If the organism is found to be highly resistant to penicillin shift should be made to the antibiotic determined to have greatest effectiveness against the infecting organism

While this is being done a surgeon skilled in intrathoracic surgery should be called in consultation, the surgeon should take over from the physician, for the treatment of choice is now surgical with either drainage, lobectomy, or pneumonectomy for those patients who do not respond promptly to antibiotics

Tumors and Cysts

The treatment of these is surgical Unless recognized too late they should be excised like neoplasms elsewhere At the present time many can be cured by localized excision, lobectomy, or pneumonectomy,

while still more can get amelioration of symptoms and prolongation of life from surgery

Pulmonary Embolism

Every effort should be made to prevent pulmonary embolism by the *early recognition of venous thrombosis by the thorough and adequate* treatment of thrombophlebitis as outlined in the preceding pages, and by the prompt recognition of pulmonary embolism when it occurs the physician must be careful not to mistake it for pleurisy or pneumonia and apply erroneous treatment For many years pathologists have pointed out that only in the presence of passive congestion does pulmonary infarction occur Prevention requires constant vigilance of the functional state of the heart and circulation and its proper treatment in any patient being treated for any illness whether there is evidence of thrombophlebitis or not In any patient with thrombophlebitis particularly in the legs or pelvis it seems wisest not to have the individual inhale and exhale deeply as in examinations of the chest, for the associated negative pressure may suck off a portion of clot which will travel to the lungs with resulting embolism

The two extremes of results of pulmonary embolism are complete silence or sudden death When pulmonary embolism has occurred prompt measures should be taken to institute the treatment of thrombophlebitis as outlined in the preceding pages to prevent further embolism

When symptoms are any more than very mild the patient should be put at complete bed rest and given 100 per cent oxygen to breathe preferably in a tent For the severe pain and apprehension morphine sulfate 8 mg subcutaneously is advised Some recommend the use of papaverine and atropine together papaverine 30 to 60 mg and atropine 1 to 2 mg both given intravenously every 3 to 4 hours to aid in overcoming the general pulmonary arteriolar spasm that may occur Pulmonary embolism of more than mild degree causes a great strain on the right side of the heart cor pulmonale therefore intravenous fluids even in the presence of shock should be given with great caution If right heart failure develops to cause more than mild symptoms venesection should be performed Occasionally an embolus is infected if it should set up an infection in the lung proper antibiotic therapy is advised Large doses of morphine should be avoided if there is severe cor pulmonale and con

gestive failure that cannot be corrected by the usual measures There is good evidence that morphine can be harmful in such cases

BIBLIOGRAPHY

1 BANYAI A "Management of Cough in Daily Practice" *Jour Amer Med Assoc* 19[illegible] cxlviii p 501

2 BARACH A L "Remissions in Bronchial Asthma and Hypertrophic Pulmonary Emphysema" *Jour Amer Med Assoc*, 1951 cxlvii p 730

3 COMROE J H Jr BAHNSON E R and COATES E O Jr "Mental Changes Occurring in Chronically Anoxemic Patients during Oxygen Therapy" *Jour Amer Med Assoc*, 1950 cxliii p 1044

4 COOKE R SHERMAN W MENZEL A CHAPIN H HOWELL C SCOTT R MYERS P and DOWNING L "ACTH and Cortisone in Allergic Diseases Clinical Serologic (Electrophoretic) and Immunologic Studies" *J Allergy* 1951 xxii p 211

5 EASTLAKE C Jr "Symposium on Inhalation Therapy Aerosol Therapy in Sinusitis Bronchiectasis and Lung Abscess" *Bull N Y Acad Med* 1950 xxvi p 425

6 FEINBERG S M "Allergy Therapy" *Jour Amer Med Assoc* 1951, cxlvii p 617

7 FRIEDLANDER S and FRIEDLANDER A S "Effect of Cortisone Administered Orally in Bronchial Asthma" *Jour Amer Med Assoc*, 1951 cxlvi 1381

8 GORDON B and MOTLEY H L "Pathological and Physiological Factors Involved in the Treatment of Silicosis in Coal Miners" *A M A Archives of Ind Hygiene and Occ Med*, 1950 [illegible] p 365

9 GORDON B MOTLEY H L THEODOS P A LANG L P and TOMASHEFSKI J "Considerations of the Clinical and Physiologic factors in the Treatment of Chronic Pulmonary Conditions" *Dis of Chest* 1951 xix p 271

10 JEGHERS H and PRICK I B "Hazards in the Therapeutic Use of Morphine" *Med Clin No Amer* Nov 1950, p 1761

11 KENNEDY B J PARE J A P PUMP, K K BECK J C JOHNSON L G EPSTEIN N B VENNING E H and BROWNE J S L "Effect of Adrenocorticotrophic Hormone (ACTH) on Beryllium Granulomatosis and Silicosis" *Am J Med*, 1951 x p 134

12 LORENZ T H "Bronchiectasis A Study of 220 Proved Cases" *Am Jour Med Sc* 1951 ccxxi p 5[illegible]2

13 MANDEL W SINGER M J GUDMUNDSON R MEISTER, L and MODERN F W S Intravenous Use of Pituitary Adreno corticotropic Hormone (ACTH) *Jour Amer Med Assoc* 1951 cxlvi p 546

14 RENOLD A E FORSHAM P H MAISTERRENA J and THORN G W Intravenously Administered ACTH *N E J Med* 1951 ccxliv p 796

15 WOODS J W MANNING I H Jr and PATTERSON C N Monilial Infections Complicating Therapeutic Use of Antibiotics *Jour Amer Med Assoc*, 1951 cxlv p 07

16 GORDON B Clinical and Physiological Aspects in the Diagnosis and Treatment of Chronic Pulmonary Diseases *Med Clin No Amer* Nov 1951 p 1695

17 IRWIN J W HENNEMAN P H WANG D M K and BURRAGE, W S Maintenance Cortisone in Intractable Asthma Preliminary Observations of Undesirable Cortisone Effects *J Allergy* 1954 xxv 201

18 OLSEN A M and CLAGETT O T The Treatment of Bronchiectasis *Med Clin No Amer* 1954 July 1019

19 CLAGETT O T KIRKLIN J W and CHILDS D S Jr The Treatment of Bronchogenic Carcinoma *Med Clin No Amer*, 1954 July 1123

o BARBER H and LAMBERTA F Treatment of Symptomatic Giant Air Cysts of the Lungs *Jour Amer Med Assoc* 1954 clvi 307

CHAPTER XLVII

DISEASES OF THE PLEURA

The pleura is frequently involved secondarily to other disease processes but only occasionally is it the primary site of disease Disease of the pleura may cause pleurisy and lead to the formation of effusion, exudate, transudate, or pneumothorax

Pleurisy

Pleurisy may be acute or chronic Acute pleurisy may be dry (fibrinous), with effusion (wet), or purulent (empyema) Chronic pleurisy may be dry or with effusion

Acute Dry (Fibrinous) Pleurisy If the causative factor is known treatment should be organized and directed toward its elimination Immediate measures consist of bed rest, which should be maintained until the temperature returns to and remains normal, and relief of pain Hot or, occasionally, cold packs to the painful area are helpful as is diathermy A tight-fitting non elastic, canvas jacket, tightly buckled over cotton padding, aids materially in limiting respiratory excursions and thus affords considerable relief Strapping with 3-inch adhesive plaster applied during full exhalation with the strips extending well on to the uninvolved side affords some splinting and gives relief Since adhesive plaster is often irritating to the skin, this should be considered a temporary expedient and removed after 3 days

Codeine phosphate, 30 to 60 mg, methadone hydrochloride, 5 to 10 mg, dilaudid hydrochloride, 1 to 2 mg, and morphine sulfate, 6 to 8 mg are all effective when given hypodermically, and any one of them may be repeated at 4-hour intervals as required There is less depression with methadone and dilaudid and consequently they are more desirable as analgesics during the daytime If cough is a factor, codeine phosphate 15 to 30 mg every 3 or 4 hours, or dihydrocodeinone (Hycodan) bitartrate, 5 to 15 mg 3 or 4 times a day, will give relief

Severe pain may require procaine hydrochloride block of the intercostal nerve supply for adequate relief Ocassionally artificial pneumothorax may be required for persistent severely painful cases

The diet should consist of easily digested foods and be high in calories and vitamins Fruit fruit juice, cereals broths fish chicken meat (except pork) cheese cooked strained vegetables purees milk and cream are excellent

Distension must be avoided and the bowels should move daily Constipation should be relieved promptly, milk of magnesia 15 to 30 cc cascara sagrada tablets 0 3 gm or the aromatic fluid extract of cascara sagrada 4 to 8 cc daily are effective The cathartic should be given on retiring for the night If relief is not secured a soapsuds enema should be given next morning

As the acute phase subsides further therapy is governed by the underlying disease if that is known Idiopathic cases with normal pulse and temperature for at least 3 days may be allowed to get up briefly and then resume normal activities gradually Since there is a possibility of tuberculosis developing later these cases should be placed on a conservative preventive regime and be checked by x ray at 6-month intervals for at least 3 or 4 years

Chronic Dry Pleurisy Chronic dry pleurisy should receive the supportive measures recommended for acute dry pleurisy Occasionally lung exercises such as blowing into bottles containing water as described under Empyema are of value Usually surgical intervention is required if adhesions cysts or fibrous bands cause respiratory difficulty When of tuberculous origin the measures recommended for the general treatment of tuberculosis are indicated

Pleurisy with Effusion

Therapeutic measures for this condition are directed toward securing relief from the immediate symptoms and ultimate control of the causative disease

Immediate measures consist of complete bed rest a highly nutritious high vitamin diet prepared to suit the patient s tastes and removal of the effusion fluid

Bed rest should be instituted promptly and maintained until the underlying process is controlled Where tuberculosis is suspected at

least 3 months bed rest is recommended Rheumatic fever patients must be maintained on bed rest until all clinical findings are normal and the sedimentation rate has fallen and remains normal on limited activity Idiopathic cases not suspected of being tuberculosis should have at least 6 weeks' bed rest after all fluid has disappeared, and activities should be resumed gradually during the next 6 months X-rays should be taken at 3 month intervals for the first year and at 6-month intervals for the next 5 years

The diet and treatment for pain or distention, if present, are the same as those recommended for dry pleurisy

The fluid should be removed and the chest cavity kept reasonably clear Aspiration is performed best at the level of the sixth interspace in the midaxillary line or in the eighth interspace behind at the angle of the scapula Many prefer the midaxillary site because, if the fluid is purulent this is a better site for a surgical drainage tube, for here kinking of the tube is less likely than in the back, and the surgeon prefers to insert the needle where pus has been found If the sixth interspace is chosen, the patient's arm on that side should be elevated and the body bent with the convexity toward the aspirating needle This posture will serve to widen the interspaces Likewise if the eighth interspace behind is chosen, the arms should be elevated and the body arched forward with the convexity toward the aspirating needle

If fluid is not obtained, puncture in another site should be tried Sometimes a site above the one selected on the basis of physical and x ray signs will yield fluid not obtained by the lower puncture

The aspiration site is painted with 1 1000 tincture of benzalkonium (Zephiran) chloride or 3 per cent tincture of iodine The skin muscle, and pleural surface are infiltrated with 2 per cent procaine hydrochloride After anesthesia has been established, a large caliber needle or a small size trocar is inserted close to the upper margin of the rib Care must be taken to avoid puncture or tear of the lung Usually, if the needle is stopped immediately after it penetrates the parietal pleura, this can be avoided During the insertion of the needle and aspiration of fluid, the patient must be watched carefully Fluid should be withdrawn slowly with frequent pauses to allow readjusting of pleural cavity dynamics Usually 500 to 1000 cc is sufficient to withdraw at one time Occasionally 1500 cc may be taken If coughing faintness pain, frothy sputum or signs of collapse appear the aspiration must be stopped and the needle withdrawn at once Immediate treatment for shock should be instituted

If slight pain or mild coughing develops but does not tend to become more severe the aspiration can be continued with caution

Following aspiration patients must be observed carefully since very rarely acute edema of the lungs may develop If acute pulmonary edema should develop morphine sulfate 8 mg and atropine sulfate 1 mg should be given subcutaneously at once followed by aminophyllin 0 5 gm intravenously

Usually 1 or 2 complete aspirations are sufficient unless there is malignancy, rarely 3 may be needed Patients with malignancy as the cause of the pleurisy may require many aspirations Immediately after aspiration x ray examination should be made to determine any underlying cause for the effusion

Treatment following removal of the fluid and amelioration of the acute symptoms is directed toward relief of the underlying disease Idiopathic cases should be followed carefully and most of them treated as if they had early tuberculosis

Chronic pleurisy with effusion should be treated as described for Empyema Most of these cases will require surgical drainage Following drainage the treatment is usually that recommended for tuberculosis

Empyema Thoracis Purulent Pleurisy

The medical treatment of empyema has assumed new importance with the advent of antibiotic therapy Penicillin streptomycin chloramphenical terramycin or aureomycin when used promptly in treating the antecedent pneumonia are effective in preventing the disease and once it has developed they are of distinct value in its treatment Medical management however should be carried out in consultation with the surgeon who will then be able to select those cases requiring surgical drainage without delay before damage of such a nature as to retard final healing has been done

Patients receive the same supportive measures and the fluid is removed by the same technique recommended for pleurisy with effusion Care must be taken to avoid air getting in during aspiration since this will prevent approximation of pleural surfaces Empyema fluid is aspirated *completely each day and replaced by isotonic saline containing the anti* biotic found most effective in inhibiting the infecting organism Usually 50 to 100 cc of isotonic saline containing 50 000 to 100 000 units of penicillin 0 5 gm streptomycin 0 5 gm terramycin or 0 5 gm aureo-

mycin as indicated by organism sensitivity are recommended The effective antibiotic is also given parenterally or by mouth as indicated and in appropriate dosage Patients should be observed closely, and improvement should become apparent within 10 days The fluid should become sterile thin, and should gradually disappear Leukocytosis, tachycardia, and fever should fall toward normal If steady improvement is not apparent in 3 to 4 weeks, surgical drainage will be necessary

Long neglected empyema with thick, purulent, difficult to aspirate fluid, or with multiple collections of fluid preventing complete aspiration, will usually require surgery

Putrid empyema caused by anaerobic organisms should receive early surgical drainage Antibiotic therapy is a valuable adjunct to drainage The effective antibiotic is given in the same manner as described for non putrid empyema

Patients recovering from chronic empyema should be taught to help re expand their lungs by deep-breathing exercises and blowing against resistance An excellent device furnishing resistance consists of two bottles connected with a tube so that water is forced from one to the other as the patient blows into the full bottle

The progress of lung re expansion should be followed by repeated x-ray studies

Hydrothorax

Transudates of non-inflammatory fluid causing respiratory embarrassment are removed by aspiration as described under Pleurisy with Effusion Treatment is then directed toward relieving the cause of the transudate

Hemothorax

Patients must be placed on complete bed rest and all activity restricted until bleeding has stopped Shock, if present, is controlled by transfusion of whole blood or plasma oxygen inhalation mild sedation or if there is severe pain morphine sulfate 8 mg, repeated in 2 hours if indicated Where peripheral vascular collapse is a severe complicating factor, morphine should be avoided Surgical intervention with ligation of bleeding arteries or lobectomy may be necessary to control serious bleeding in some cases

Once the bleeding has stopped the patient should be observed for signs of respiratory distress and increased intrathoracic pressure If these are not present aspiration is best delayed to the second or third day, as blood coagulates very slowly in the pleural cavity fibrin clots will not be present to hinder flow of blood through the aspirating needle The blood should then be aspirated until the pleural space is dry Usually no more than 500 cc is taken off at one time Reactions are more prone to occur if aspirations are larger If there is evidence of recurrent hemorrhage or if the patient develops pain or a feeling of tightness in the chest air should be cautiously introduced to make the pressure more nearly equal Approximately one third of the amount of fluid removed should be replaced by air After each aspiration 100 000 units of penicillin are injected into the pleural space as a prophylactic against infection

The lung should be permitted to re expand If expansion does not occur after several weeks operative removal of blood clots and occasionally decortication of the lung must be performed

Chylothorax

Treatment should be directed toward the primary cause Occasionally surgical removal of constricting bands of scar tissue or x ray therapy to enlarged obstructing glands will give relief Traumatic tear or rupture of the thoracic duct may require ligation

If pressure symptoms develop aspiration will give relief Patients with considerable loss of chyle are benefited by receiving retransfusion of the sterile aspirated chyle

Cholesterohydrothorax

Aspiration is necessary to clear out the pleural cavity and open the way for lung expansion Since the formation of cholesterol crystals occurs in long standing pleural fluid the pleural cavity should be aspirated as completely as possible

Pneumothorax Hemopneumothorax Hydropneumothorax Pyopneumothorax

Air or air associated with fluid blood or pus in the thoracic cavity

may occur spontaneously following the rupture of an emphysematous bleb or following trauma or disease

Spontaneous pneumothorax without associated disease is a relatively benign condition which heals readily In most cases all that is required is a few days rest If cough or pain is present, codeine phosphate, 30 mg., is helpful The lung should be watched carefully, and if it shows no tendency to re expand after 2 weeks, cautious aspiration of air is advisable Should the ruptured bleb or tear in the lung lead to hemothorax, the blood should be completely aspirated at an early date, if it is allowed to remain for long, clotting may occur and interfere with lung re expansion

Pneumothorax resulting as a complication of disease is a serious affair Patients must be on complete bed rest and kept as quiet as possible Morphine sulfate 6 to 8 mg subcutaneously, is recommended if there is much restlessness or if pain is severe Occasionally strapping the affected side with adhesive plaster is helpful in these patients Cough may be controlled with codeine phosphate 30 mg, or dihydrocodeinone (Hycodan) bitartrate, 5 mg every 3 or 4 hours If fluid is present, it should not be removed for at least 2 weeks unless pressure symptoms appear If these develop, sufficient fluid is taken off to secure relief If there is pus, it should be aspirated and penicillin instilled as recommended for empyema In pneumothorax caused by tuberculosis no effort should be made to re-expand the lung Pyopneumothorax of tuberculous origin should not be aspirated, unless severe pressure symptoms appear

Tumors

Treatment is palliative Repeated aspiration may afford temporary relief Occasionally replacement of fluid by air or oxygen is helpful

Meigs Syndrome

Complete aspiration of the hydrothorax followed by operative removal of the ovarian fibroma is curative

CHAPTER XLVIII

DISEASES OF THE MEDIASTINUM

Mediastinitis

Acute mediastinitis is usually secondary by extension from neighboring structures — the neck lungs pleura pericardium lymph nodes or spine — or from trauma from penetrating wounds of the chest wall or instrumentation of the trachea bronchi or esophagus

Acute non suppurative mediastinitis occurs by extension from inflammation of the pleura pericardium lungs or the neck Ordinarily it requires no specific treatment other than that given for the underlying condition Dysphagia may require the use of a liquid diet for a few days For pain and cough codeine phosphate 30 to 60 mg may suffice Meperidine (Demerol) hydrochloride in doses of 50 to 100 mg or morphine sulfate 15 mg should be given both hypodermically When rheumatic fever is the cause of the pericarditis and associated mediastinitis salicylates in the form of sodium salicylate or acetylsalicylic acid should be given in dosage as outlined under Acute Rheumatic Fever

In acute suppurative mediastinitis an attempt should be made when the lesion is accessible and particularly if there is localization with abscess formation to drain surgically Aspiration by needle may be attempted but great care must be used lest the infection be spread to contiguous structures Parasternal incision and drainage is the method of choice for anterior mediastinal abscesses A solution of the antibiotic effective against the infecting organism should be injected into the cavity after it has been drained and the drug should be given in adequate dosage for its systemic effect

Chronic mediastinitis may result from acute suppurative mediastinitis but usually it is seen as the result of infection with one of the causative factors of chronic infectious granulomata such as tuberculosis syphilis actinomycosis or blastomycosis

Vol VIII 353

In tuberculous mediastinitis, particularly in children, adequate rest, fresh air, and a high calorie, high vitamin diet usually suffice for treatment Unless the process is severe, or there are associated pulmonary lesions or other considerations for its use, streptomycin and para amino salicylic acid therapy is usually not needed for this type of tuberculosis

Syphilitic mediastinitis responds readily to the usual antisyphilitic therapy

The treatment of actinomycosis or blastomycosis of the mediastinum should be carried out as outlined for these diseases

Cysts

Dermoid cysts and teratomata arise most commonly in the anterior mediastinum Though present from childhood and slowly growing they are accessible to surgical removal and this should be carried out Excision is advisable because they may grow to large size causing compression symptoms, they may become infected secondarily with abscess formation or malignant degenerative changes may occur in them

Tumors

Other than the cystic types described in the preceding paragraph, tumors of the mediastinum may be considered under the headings benign and malignant

The benign tumors include aneurysm of the aorta or of the pulmonary artery, for which there is no satisfactory treatment Wiring of the aneurysm might be undertaken but results are not always good Thyroid adenomata, parathyroid adenomata and thymic gland enlargement from any cause although locally benign often cause pressure symptoms and/or systemic manifestations of hyperthyroidism, hyperparathyroidism, or possibly myasthenia gravis they require surgical removal the former after proper pre operative preparation with a thiouracil compound and iodine as outlined under Hyperthyroidism Other benign tumors of the mediastinum include fibromas and neurofibromas which occur chiefly in the posterior mediastinum as well as chondromas xanthomas and lipomas Each of these types should be removed surgic

ally when that is possible if they are causing symptoms In skilled hands today the risk of surgical exploration of the thorax is no greater than that of other body cavities

The malignant tumors of the mediastinum which usually are limited to the lymph nodes may be placed in the broad category of the lymphoblastomata These include chiefly Hodgkin s disease the leukemias and lymphosarcomata They are not amenable to surgical removal but specimens may be excised for biopsy Treatment should be palliative with high voltage x ray or nitrogen mustard urethane anti folic acid derivatives or other measures as outlined in the section on Diseases of Lymph Nodes and under Diseases of the Blood The use of these agents is unfortunately not curative (See also Bronchiogenic Carcinoma)

Mediastinal Emphysema

Mediastinal emphysema may occur as (1) the result of trauma or therapeutic procedures or (2) from the spontaneous rupture of an emphysematous bleb of the lung or pulmonary alveolus

Mediastinal emphysema resulting from the trauma of a therapeutic *procedure is usually secondary to pneumothorax with the air in the* pleural space dissecting its way into the mediastinum It can result however from a foreign body penetrating through the chest wall or from air making its way from the neck and suprasternal spaces as in subcutaneous emphysema of the neck Ordinarily this requires no treatment except for control of pain or cough for which codeine phosphate 30 to 60 mg every 3 or 4 hours may suffice If tension pneumothorax develops as from a sucking wound with ball valve action a needle should be introduced into the involved side with attached rubber tubing extending 3 *to* 4 cm *below water level in an appropriate vessel after* pressure equilibrium has been reached with appropriate expansion of the involved lung the wound should be closed tightly by surgical means

Sometimes following attempted thoracentesis or with the introduction of air for therapeutic pneumothorax in the treatment of tuberculosis air will dissect into the interstices of the mediastinum with emphysema resulting As with traumatic emphysema this usually requires no treatment other than bed rest and measures to control cough and pain unless tension of pneumothorax develops in which case treatment should be *as outlined in the preceding paragraph*

Acute Spontaneous Interstitial Emphysema Hamman's Syndrome

The treatment of spontaneous interstitial mediastinal emphysema requires primarily its proper recognition so that it is not treated erroneously as angina pectoris or as acute coronary thrombosis It requires no treatment other than several days of bed rest with observation and measures to combat the pain Codeine phosphate, 30 to 60 mg, repeated once or twice by hypodermic injection is usually sufficient, for severe pain morphine sulfate, 15 mg as an initial injection may be necessary The condition will resolve itself in a few days from resorption of the air

Mediastinal Flutter

Mediastinal flutter is a condition of mobility of the mediastinum with symptoms of pain dyspnea cough and sometimes, syncope resulting from a sudden shifting of the mediastinum of more than a minor degree from its central position It is the acuteness of the shift that causes distress for it is remarkable how much the mediastinum and its structures may often be moved to the right or left when the shift occurs slowly — as from a gradually accumulating pleural effusion — with little in the way of the symptoms above The treatment of acute mediastinal flutter is to remove the blood effusion or air that is pushing the mediastinum to the opposite side Atalectasis, unless the collapse is massive seldom produces symptoms of acute mediastinal flutter When massive collapse produces such symptoms bronchoscopy with an attempt to re inflate the lungs may become necessary

BIBLIOGRAPHY

1 HAMMAN L Spontaneous Mediastinal Emphysema *Bull Johns Hopkins Hosp*, 1939 LXIV p 1
2 KEEFER C S Acute and Chronic Mediastinitis A Study of 60 Cases *Arch Int Med*, 1938 LXII p 109

PART XV

DISEASES OF THE KIDNEY AND URINARY TRACT

CHAPTER XLIX

DISEASES OF THE KIDNEY

Acute (Hemorrhagic) Bright's Disease. Acute Glomerulonephritis

The majority of patients with acute hemorrhagic Bright's disease are only mildly ill. Slight fever is frequent but it may be present only during the course of the upper respiratory tract infection that nearly always antedates the development of this form of Bright's disease. If fever is present or positive throat cultures of streptococci are present it is well to give penicillin in the usual dosage. Usually, malaise is moderate. Edema is the rule but in this form of the disease it is only slight to moderate and rarely needs any special management. Urinary symptoms may be lacking except for some evidence of blood in the urine or there may be frequency, urgency and discomfort in the bladder or lumbar regions and scanty bloody urine. Somnolence and headache are common. Convulsions may occur, especially in children. Many patients exhibit the symptoms of cardiac decompensation if carefully looked for; this is to be treated with digitalis in the usual way. The therapeutic problem is essentially one of symptomatically treating the symptoms already enumerated, retarding or stopping the progression of the renal lesion and, if possible, leaving the patient free subsequently of any evidences of a continuing renal lesion or at least with only a minimal one compatible with long continued good health. Of great importance is the prompt and thorough treatment of those infections that often antedate and may cause the renal lesions by using the appropriate antibiotic which should be used also in the acute phase of the renal disease.

Rest To attain the end just expressed, bed rest remains one of our most effective methods This must be continued, often for many weeks until blood disappears from the urine sediment or is reduced to only a few red blood cells not increased by moderate physical activity This is the criterion of successful treatment

How long should the patient be kept in bed? Certainly until edema disappears, fever ends, any signs of cardiac insufficiency disappear and after this, until red cells and albumin in the urine disappear or become very slight in amount and are not increased by moderate exertion In some patients however, small amounts of blood persist in the urine for weeks, after continued bed rest, apparently ineffective in stopping such slight continued hematuria, a trial period out of bed should be instituted and if blood does not increase in the urine, this period may be continued Then trial of moderate physical activity, especially early bathroom privileges should be instituted In an occasional patient a few blood cells in the urine will persist for years before any other symptoms of Bright s disease appear

If the patient has a continued lowered renal function as measured by any of the tests, his out-of-bed periods and physical activity, with trial periods to find out their effects should be managed as has just been described in relation to blood in the urine

A patient with any type of Bright's disease should be guarded against chill, which, if it occurs, may precipitate exacerbations The feet, especially of the patient who is sitting up should be protected from cold by woolen socks or stockings if his feet are on the floor Too much fresh air often chills the patient even when he remains in bed, he should be kept comfortably warm In general the patient with Bright's disease needs shoulder wraps adequate blankets both under and over the patient and a long sleeved, high necked pajama or nightgown when the weather is cold Prevailing styles, especially those for women of very thin stockings and thin, sleeveless, low cut night garments, should be prohibited

Diet During the first few days of the acute phase of the disease the dietary intake is usually limited by nausea and vomiting Fruit juices tea, milk and sweetened drinks are usually tolerated This should be followed by a more liberal diet as soon as possible If nausea prevents any food intake intravenous 10 per cent glucose should be given in a daily amount of 1000 to 1500 cc Shortly this decreased food intake should be shifted to a diet such as that outlined below which is low in protein about 26 gm and contains approximately 120 gm of fat and 250 gm

of carbohydrate totaling about 2000 calories A moderate amount of salt may be added to make the diet palatable, a strictly salt free diet is not needed and with rare exceptions these patients are better off without it Few patients will object to a salt poor diet

26 GM PROTEIN LOW-SALT (2 GM) DIET

Food	*Amount*	*Protein*	*Fat*	*Carbohydrate*	*Calories*
Cream	200 cc	4.4 gm	80.0 gm	6.0 gm	761.60
Butter	60 gm	.6	51.0		461.40
Bread	90	8.28	1.17	47.79	34.81
Sugar	65			65.0 "	260.00
Potato	100	2.5	0.1	20.9	94.50
Orange	50	0.4	0.1	5.8	25.70
Oatmeal	150	4.1 "	0.75	17.25	92.55
Lima beans	50	2.0	0.15	7.3	38.55
Corn	100	2.8	1.2	19.0 "	98.00
Pineapples (canned)	50	0.2	0.35	18.2 "	76.75
Peaches or pears (canned)	100	0.7 "	0.1	10.8	46.90
		26.08	134.9	218.04	2190.76

Example of a daily menu for such a diet follows no salt is to be used in it

Breakfast	*Luncheon*	*Supper*
50 gm baked apple	00 gm potato	100 gm sliced tomato
30 gm shredded wheat	100 gm corn	100 gm macaroni
30 gm bread	30 gm bread	30 gm bread
10 gm butter	10 gm butter	10 gm butter
150 cc coffee with 40 cc cream and 25 gm sugar	150 cc tea with 20 cc cream and 10 gm sugar	150 cc tea with 40 cc cream and 25 gm sugar
	dessert made of 75 gm pine apple and 50 cc cream	100 gm canned pear

As soon as possible the patient with acute Bright s disease should be given a diet well balanced in carbohydrates fat and vitamins with 60 to 75 gm of protein all of which should total 2000 to 2500 calories if the patient is not considerably below average size For many reasons including possible presence of edema weight is not a satisfactory guide for calorie intake in these patients Large patients should receive fewer calories than ones more by increased carbohydrate and fat in the diet Such a diet can be arranged easily on the basis of the schema of the following 75 gm protein diet

75 GM PROTEIN DIET

Food	*Amount*	*Protein*	*Fat*	*Carbohydrate*	*Calories*
Milk	400 cc	13 2 gm	16.0 gm	20.0 gm	76 8
Cream	60 cc	1 3	24.0	1.8	228.4
Olive oil	0 cc		20 0		180.0
Butter	45 gm	0.4	38 2		345.4
Eggs	2	13.4	10 5 "		148 1
Sugar	25			25.0	100.0
Cereal	150	3 5 "	0.4	17 6 "	87 2
Bread	60	5 5	0 7	31.6	154 7
Macaroni	100	3.0	1 5 "	15.8	88 7
Vegetable	300	6 0		30 0	144.0
Cocoa	5	1.0 "	1.4	1.8	3.8
Meat	150	28 5	18.0		276.0
		76 8	130 7	143.6	2033 1

An example of a daily menu for this diet

Breakfast	*Forenoon*	*Dinner*	*Afternoon*	*Supper*
1 orange 150 gm cream of wheat with 20 cc cream 1 scrambled egg 20 gm toast 15 gm butter 150 cc coffee with 20 cc cream 10 gm sugar and 25 cc milk	200 cc milk	100 cc milk soup 75 gm roast beef 100 gm potato 100 gm carrot 20 gm bread 15 gm butter custard (milk 100 cc) (sugar 10 gm) (egg 1) 150 cc tea with 25 cc milk 5 gm sugar	150 cc orangeade or lemonade with 5 gm sugar	50 gm chicken 100 gm. spinach 100 gm baked apple with 5 gm sugar and 20-cc cream 150 cc tea with 10 gm. sugar and 20 cc milk 0 gm. bread 15 gm. butter

Tea and coffee with cream and sugar once a day are allowable components of the limited diets just described, their fluid bulk being counted in the 24-hour fluid allowance for the patient

Fluid Intake Fluid should be measured and should consist of water, fruit juices milk tea and coffee The amount should be at neither extreme The large amounts formerly given to patients with acute Bright s disease were probably harmful and should not be used If there is marked edema or nausea, it is well to restrict fluids for a few days giving not more than 1000 cc in 24 hours If nausea is marked with accompanying vomiting no fluid should be given by mouth, ice may be

sucked to relieve throat dryness To prevent dehydration, intravenous 5 to 10 per cent glucose in normal saline solution should be given as long as nausea persists — 1000 to 2000 cc each 24 hours as needed but not more than 1000 cc at one time If vomiting is marked, much fluid will be lost this should be replaced by increasing the amount of the transfused fluid until dehydration has been counteracted Another guide to fluid intake is the blood urea level for if fluid intake is greatly restricted this will increase The fundamental principle that protein, salt, and water restriction are intended to lessen the work of the kidney should be kept in mind in planning the diet and fluid intake of patients with acute Bright s disease, there is optimum level to be attained for each by attention to the 24 hour output of urine and the level of urea or of non protein nitrogen in the blood

Hypertension When this occurs treat as recommended on pages 744 5

Drugs Digitalis preparations should not be used unless there is a complicating cardiac decompensation in which case these patients should be managed as described in the chapter on Chronic Heart Disease except that mercurial diuretics are contraindicated during the acute hemorrhagic phase of the disease In the beginning of acute Bright s disease especially when there is fever penicillin should be given since so often one of the coccic organisms especially the streptococcus is the cause of the renal lesion Penicillin terramycin or aureomycin also should be used in treating the antecedent or accompanying infection especially an infection of the upper respiratory tract Mild laxatives such as cascara sagrada 0 3 gm should be used if the patient s bowels do not move satisfactorily Vigorous catharsis is no longer advised

Uremia If, along with marked oliguria or anuria evidences of uremia develop treatment needs to be directed primarily toward lowering the protein content of the diet by using the 26 gm protein low salt diet already described and the dilution in or removal from the circulation of various retained substances causative of uremic symptoms especially the non protein nitrogen components or the chemical correction of some of them as by the use of alkalis to offset acidosis This removal can be accomplished most satisfactorily by use of the artificial kidney if one is available If not continuous peritoneal irrigation with large amounts of bland hypotonic Tyrode s or Ringer s Solution is the next most effective procedure These methods especially the use of the artificial kidney often produce dramatically satisfying results If neither of these methods is available and practicable, continuous tubal irrigation of the gastro-

intestinal tract with a bland hypertonic solution will remove from the blood stream a considerable amount of injurious substances and may be beneficial

It is very important to check what is going on during these procedures by frequent determinations of the amount of metabolites, both electrolytes and non electrolytes, contained in the patient's blood Often an injurious deficiency of sodium and chloride will develop, especially when there has been continued vomiting, it should be made up by transfusion of normal saline with 5 per cent glucose and/or the ingestion of sodium chloride Also, when acidosis is detected, it should be corrected by the ingestion of sodium bicarbonate or by intravenous injections of 5 per cent sodium bicarbonate or ⅙ molar sodium lactate Some help in combating acidosis is secured by lowering the elevated phosphate by giving aluminum hydroxide gel, such as Amphogel, Gelusil, or Basalgel in doses of 10 to 15 cc every 2 or 3 hours The aluminum forms insoluble phosphate and effectively lowers the phosphate intake, this in turn leads to a lowered serum phosphate and consequently less acidosis It is important at all times to be sure that any developing dehydration is corrected by adequate water replacement by mouth, by rectum, or by slowly given intravenous injections of normotonic solution and/or blood plasma It is equally important, however, not to carry fluid intake to the point of causing edema, the possible presence of edema should be watched for by frequently inspecting the patient's subcutaneous tissues and by weighing, if the patient is not too ill, as is so often the case For weighing these patients, a mechanism is necessary so that a stretcher can be put on the scales Even better would be a platform on which the patient could be weighed in bed

Potassium may increase in the blood serum and cause serious toxic effects When this occurs the potassium should be removed by the use of a cation exchange resin Hydrogen saturated amberlite without potassium may be given orally or by rectum in a dose of 50 gm daily It effectively lowers the potassium without disturbing other electrolytes Bleeding is desirable as an emergency treatment if the removed blood can be replaced by blood from normal individuals The patient's own red blood cells can be used for replacement if they are removed from their serum and resuspended in plasma or normal saline solution Bleeding should be a measure only for a critical situation while other measures already outlined, are being carried out

Restlessness, if disturbing, should be controlled by sedatives, if it is

extremely marked morphine sulfate should be given frequently by hypodermic injection in doses of 6 to 10 mg. In view of the defective excretion in these patients with small urine output smaller than usual doses of almost all medicaments are needed to get desired pharmacological action, while average normal doses may prove toxic. Instead of morphine chloral hydrate, 1.0 to 2.0 gm. well diluted in fruit juice or paraldehyde in olive oil in doses of 10 to 20 cc. given preferably by rectum may be used. The shorter acting barbiturates pentobarbital (Nembutal) and secobarbital (Seconal) in doses of 0.1 to 0.2 gm. may prove very helpful in reducing restlessness and muscle twitching. They are also helpful in controlling convulsions. Usually a dose of 0.2 to 0.4 gm. intravenously is satisfactory.

Muscle twitching if disturbing may be controlled by intravenous calcium therapy: use 10 to 15 cc. of a 10 per cent solution of calcium chloride or better 15 to 30 cc. of a 10 per cent solution of calcium gluconate.

Nausea and vomiting are frequently controlled by chlorpromazine 25 to 50 mg. intramuscularly initially followed by 25 to 50 mg. by mouth every four hours.

Oliguria and Anuria. If oliguria commences the general methods of management in regard to rest, diet and fluid intake as already described for the more severe forms of this disease should be continued; if they have not been instituted they should be commenced. It is very important not to increase fluid intake with a decreasing urine output but rather to decrease it. The former practice of flushing the kidneys by a large fluid intake should not be followed. Only enough fluid should be given to prevent dehydration as judged by the appearance of the tongue and skin and the feel of the subcutaneous tissues. If oliguria becomes marked or anuria develops this fluid restriction should be continued and the treatment should be as previously described for uremia. Diuretics should not be given to patients with this form of Bright's disease, however marked the decrease in urine flow becomes. Hot cloths or warming pads to the loins may possibly be helpful; at any rate they will do no harm if care is taken to prevent burning the skin.

Anemia, if moderate, should be treated with ferrous sulfate or gluconate, 0.2 to 0.3 gm. 3 times a day; if it is marked, transfusions of blood should be given. It is an interesting fact that although hematuria may persist, anemia of more than very slight degree is very unusual unless there is a cause in addition to the acute glomerular lesions in the kidney.

Acute, Subacute, and Chronic Edematous Bright's Disease
Nephrotic Syndrome

The chief object of treatment for the edematous type of Bright's disease is to reduce the edema while maintaining as good general nutrition as possible and to avoid infections or, if they do occur, to treat them with antibiotics as soon as possible In the acute phases of this type of Bright's disease the patient should receive the form of general management described in the previous section In addition, the edema requires special attention removing excess fluid from the body and elevating the plasma albumin, whose deficit is considered a primal cause of the edema are the essential steps at this stage

Bed rest Edematous patients of this type should have bed rest, continued until edema abates or until it seems evident that it is going to persist relatively unchanged for a long time Some of these patients however, soon become uncomfortable in bed, even when they are propped up, for them a cushioned chair, with a foot-rest arranged so that the feet and lower legs are not too dependent, should be used The possibility of pressure decubitus must always be kept in mind, since if detected at its beginning, it can be kept from progressing by suitable changes in position and by the use of air or gauze rings to avert damaging localized pressure For many of these patients bathroom privileges should be allowed even when getting there requires a short walk

Often bed rest after a time decreases the patient's morale, lessens his appetite, and deteriorates his general condition If so, the physician should allow the patient to be out of bed and even to walk about some, watching to see if this increases the edema and albuminuria and, if not, gradually permitting more activity Many patients are definitely better when this change in regime is instituted Some of them can, with safety, become ambulatory patients if their activity is guided so as to prevent any fatigue, recovery from which is slow, and to keep the fluid in the feet and lower legs from accumulating to the extent of inducing a brawny chronic inflammation Fortunately, many have no cardiac disability, even when the condition has continued over a long period of time, the cardio-circulatory system remains efficient, partly because hypertension develops, as a rule very late in the progression of this form of renal disease usually after the edema of renal origin has decreased markedly or disappeared, and so physical activity does not disturb the cardio-circulatory mechanism

The cautious and experienced physician can, by observation and the

method of trial and error vary the patient s restrictions decreasing or increasing them as seems desirable and thereby do much toward re stricting progression of the disease while keeping his patient in a con tented frame of mind and still carrying on all needed therapeutic management

Diet The dietary requirements of patients with edematous type of Bright s disease make it difficult to prepare a diet that the patient will continue to eat in adequate amount Such a diet should contain a large amount of animal protein and a small amount of sodium and chloride a low amount of sodium is especially important Few patients will eat such a diet over a long period of time they soon tire of large amounts of meat with almost no salt The patient should be encouraged however *by physician nurse and family to eat everything offered at each meal* The large amount of protein necessary presents less of a problem than the great salt deficiency Physician and dietitian must as a rule compromise and give the patient in the long run less meat and more sodium and chloride than is considered ideal for after all no diet that the patient *cannot be persuaded to eat steadily in adequate amount can be termed* satisfactory The patient s wishes even whims must be catered to continuously and so met that the diet remains high in protein and low in sodium and chloride or at least relatively so

For these patients it may be a good idea to try for a week or ten days a diet of very low sodium chloride content and not seek at this time to give them a large amount of protein Such a diet is given below followed by a sample menu for a day and directions for making salt free bread and dialyzed salt free milk

70 GM PROTEIN LOW SALT (0 2 GM) DIET

Food	*Amount*	*Protein*	*Fat*	*Carbohydrate*	*Calories*
Unsalted milk made with Lonalac	60 gm (dry weight)	16	17	23	309
Butter	75 gm		61		549
Unsalted bread	120	11	4	60	320
Sugar	15			15	60
Potato	200 "	4		40	176
Unsalted cereal	15 (dry weight)	2		11	52
Vegetables	700 gm	7		87	376
Fruit juice	600 cc			60	240
Meat	120 gm	30	18		282
		70	100	296	2364

Breakfast	*Dinner*	*Supper*
½ medium grapefruit	2 oz hot roast beef	2 oz cold lamb
1 glass orange juice	½ cup mashed potato *	1 medium baked potato
½ cup cooked whole grain cereal *	½ cup new cabbage *	⅓ cup green beans *
2 slices toast **	½ large tomato with lettuce and 1 tablespoon mayonnaise *	salad of raw carrot sticks lettuce and mayonnaise
2 squares butter	1 sliced medium orange	1 sliced banana
1 cup coffee	2 slices bread *	½ pint milk *
1 tablespoon sugar	2 squares butter	2 slices bread *
½ pint milk		2 squares butter *

*Afternoon drink**

1 glass pineapple juice

* prepared without salt
** salt free bread prepared as described in following paragraph
dialyzed salt free milk prepared as described below

Salt free bread can now be purchased in many city food stores or bakeries or it can be made as follows to yield a 1-pound loaf

Salt free Bread

⅔ cup lukewarm water
½ yeast cake
1½ tablespoons sugar (white)
1½ tablespoons Spry or Crisco
2⅓ cups Gold Medal flour

Sift and mix the dry ingredients Cut in the fat having finely divided it Crumble the yeast cake in ¼ cup of the lukewarm water Add yeast and flour to the water mixing them thoroughly Put mixture on flour board and knead thoroughly adding more flour if necessary Place in a bowl well greased with salt free butter or other fat having also greased the top of the dough Cover bowl with clean towel place in a warm place and allow to rise until double in bulk Take from bowl place on floured board and knead again Place in a greased loaf pan and allow to rise again until double in size Bake in a moderately hot oven for about half an hour Cool and slice

Salt free Dialyzed Milk

Use dialyzed milk powder (Lonalac) and dissolve 30 gm of this in ½ pint of water

The idea in using this very low salt diet is to see whether the patient will respond by marked loss of edema when sodium and chloride are

almost omitted from the diet If this loss results such a diet should be continued until edema has largely disappeared then a diet with more salt and more protein should be substituted If edema does not decrease then it will be wise to return at once to a diet high in protein as high as the patient can be induced to eat but containing considerably more sodium and chloride than the diet just described more of these than is considered to be ideal yet a quite low sodium content can still be attained by preparing food items without adding salt With more sodium and chloride the diet usually will be much more palatable For some patients even more sodium and chloride will be needed as an inducement to eating more protein A weighed amount of salt (i e weighed in the kitchen) in a shaker which the patient can add where he wishes often proves a dietary morale builder and still considerably restricts intake of sodium and chloride In other words dieting should be on a trial and error basis to attain as great a decrease in edema as possible Some patients find salt substitutes helpful These usually contain potassium chloride ammonium chloride and potassium citrate Neocurtasal disalt and cosalt are three common commercially available salt substitutes Unfortunately most patients eventually find these products unpalatable unless used very sparingly

A diet very high in protein can be planned readily by doubling the amount of meat eggs milk vegetables and bread in the 70 gm protein diet given on page 597 so that it will contain 142 gm of protein A high protein diet is shown in the schema on page 600 The amounts of food given in such diet schemas are of course to be divided into three meals with or without intermediary luncheons according to the taste of the patient with daily variations in the selected foods to prevent monotony as far as possible

If the patient is unable to eat so much meat and other protein containing foods a 109 gm protein diet can be obtained by increasing by half the amount of meat eggs milk vegetables and bread in the 70 gm protein diet this is shown in the schema on page 600

Since it is believed by some that animal protein is more effective than vegetable protein in decreasing the deficiency of plasma protein in these patients a diet with increased animal protein can be constructed by *doubling the amount of milk eggs and meat in the 70 gm protein diet* while not changing the amount of vegetable and bread this will give 130 gm of protein largely non vegetable in origin as shown in the schema on page 601 *for a 130 gm protein diet*

14 GM PROTEIN DIET

Food	*Amount*	*Protein*	*Fat*	*Carbohydrate*	*Calories*
Milk	800 cc	6.4 gm	3 0 gm	40 0 gm	553.6
Cream	60 cc	1 3	24 0	1.8 "	2 84
Olive oil	0 cc		0 0		180.0
Butter	45 gm	0.4	38		345.4
Eggs	4	26 8	21.0		296.2
Sugar	5 gm			5.0 "	100.0
Cereal	150	3 3	0.4 "	17 6 "	87 2
Bread	1 0	11 0	1.4	43	309.4
Macaroni	100	3 0	1 5	15.8	88 7
Vegetable	600	1 0		60.0 "	288.0
Cocoa	5	1 0	1.4	1 8	3.8
Meat	300	57 0	36 0		552.0
		14	175 9	5 "	305 7

109 GM PROTEIN DIET

Food	*Amount*	*Protein*	*Fat*	*Carbohydrate*	*Calories*
Milk	600 cc	19 8 gm	24 0 gm	30 0 gm	415.2
Cream	60 cc	1 3	24.0	1.8 "	2 84
Olive oil	20 cc		20.0		180.0
Butter	45 gm	0.4	38 2		345.4
Eggs	3	20 1	15 7		221 7
Sugar	25 gm			25.0	100.0
Cereal	150 gm	3 3	0.4	17 6	87.2
Bread	90 gm	8	1 0	47.4	239.4
Macaroni	100 gm	3.0	1 5 "	15 8 "	88 7
Vegetable	450 gm	9 0		45.0 "	216.0
Cocoa	5 gm	1 0	1.4	1.4	2 .2
Meat	225 gm	42 7	27 0		313.8
		108 8	153	184 0	558.0

Since in all of the diets just described except the 70 gm protein one, the caloric content is probably too high for most patients (it ranges from 3052 in the diet containing 142 gm of protein to 2558 in the one containing 109 gm of protein) and since many of these patients are being kept in bed or are permitted only moderate physical activity caloric values can be and probably should be lowered as necessary by omitting olive oil and by reducing the amounts of cream butter, cereal macaroni, or other carbohydrates this will decrease only very slightly the important protein content of these diets while reducing their caloric content

130 GM PROTEIN DIET

Food	*Amount*	*Protein*	*Fat*	*Carbohydrate*	*Calories*
Milk	800 cc	26.4 gm	32.0 gm	40.0 gm	553 6
Cream	60 cc	1 3 "	24.0	1 8	228.4
Olive oil	20 cc		20.0 "		180.0
Butter	45 gm	0.4 "	38 2		345.4
Eggs	4	26 8	21.0		296 2
Sugar	25 gm.			25.0	100.0
Cereal	150	3 3	0.4 "	17.6	87 2
Bread	60	5 5	0 7	31 6	154 7
Macaroni	100	3.0	1 5	15.8	88 7
Vegetable	300	6.0 "		30 0	144 0
Cocoa	5	1.0	1.4	1 8	3.8
Meat	300	57.0	36.0		55 .0
		130 7	175	16, 6	2 54.0

The physician nurse and dietitian must always keep in mind that it is not the diet on the tray or table that counts but what the patient actually eats Remember too that sodium is not being restricted by limiting the amount in the diet if the patient is receiving such medicaments as sodium bicarbonate sodium salicylate sodium bromide sodium benzoate (also a constituent of oleomargarine) sodium nitrite or nitrate *sodium borate sodium thiocyanate a laxative containing a sodium salt* such as phosphate of soda Glauber s salts (sodium sulfate) or parenterally given fluids such as normal saline solution blood or plasma et cetera The amount of sodium being given in any of these ways should be added to that in the diet to determine the patient s actual daily intake of sodium Such medicaments should be excluded if a diet very low in sodium is a factor in the anti edema treatment

Fluid Intake The former practice of great restriction of fluid intake is no longer advised for patients with edematous type of Bright s disease There are two plans for fluid intake now in general use One is to give 1200 to 1500 cc of fluid consisting of the fluid elements in the diet plus the needed amount of added water using water low in salt content (if necessary selected spring or bottled water low in sodium content or of distilled water) If the patient complains of thirst especially while sweating in hot weather more water should be given Also an edematous patient not infrequently becomes dehydrated as shown by dry mouth shriveling of a dry tongue or a non sweating skin in those areas devoid of edema these patients with dehydration will need a considerably in

creased fluid intake until their dehydration disappears

The other plan is to give a fluid intake of 2000 to 4000 cc unless cardiac failure develops in which case the fluid intake should be reduced until congestive failure has been removed by appropriate cardiac therapy Then fluid intake may be increased again but it must be controlled by careful observation so that a developing congestive failure may be detected early Usually congestive failure is indicated by an abrupt decrease in the previous level of urine excretion by an increase in the patient's weight, or by hepatic discomfort and possibly local tenderness and palpable enlargement of the liver Cardiac decompensation would undoubtedly be much more frequent in patients with the edematous type of Bright's disease were it not true that these patients in the stage of edema very seldom have hypertension These larger amounts of fluid can be given safely when the patient is on a low-sodium diet even during cardiac decompensation

There are no regulations about the kind of fluid to be given except that a drinking water with high sodium content should not be used Though claimed to be of great value for patients with diseased kidneys various waters from special springs have no virtue beyond their purity and a needed low-sodium content and even the latter is not actually found in all of them

Efforts to Increase the Osmotic Pressure of the Circulating Blood Since the edema in this type of Bright's disease is thought to result very largely from the lowered osmotic pressure of the circulating blood incident to its decreased content of protein chiefly its decreased content of albumin — i e hypoalbuminemia — and since this hypoalbuminemia is caused by the continued daily excretion into the urine of large amounts of albumin — i e albuminuria — obviously an effective therapy should be based on either (1) decreasing the albumin loss in the urine or ( ) increasing the albumin level of the blood or substituting for its albumin some bland substance of approximately the same molecular weight. Either method seeks to restore osmotic pressure to normal

Unfortunately we know of no satisfactory way to decrease the excretion of albumin into the urine All we can do is to hope for a healing process in the kidney aided by the general methods of treatment already outlined, or await that change in the usual progression of the renal lesion into one in which the albuminuria lessens or almost ends and the renal edema disappears, an evolution which can be excepted but which is unfortunately accompanied by an increasing retention of nitrogenous

substances and an eventual azotemia that will be lethal On the fortunate side are the facts that the healing process occurs fairly often in this type of Bright's disease and that often there is a considerably long period of slight albuminuria and no renal edema before azotemia begins

To increase the plasma albumin level toward normal use the *diets high in protein* given above Unfortunately high protein feeding is only very moderately effective in elevating plasma albumin and so we need to resort to other procedures Of these the intravenous injection of *purified human albumin* would seem most likely to be effective Purified human albumin has been prepared and its intravenous use has been tried As first used its salt content was too high and so a *salt poor human albumin* was made available This can be given without any disturbing reactions if given slowly but it was found that continued daily injections would be needed since this albumin disappeared rapidly from the circulation and much of it was excreted into the urine when there was a renal lesion causing marked albuminuria Consequently an induced increase in plasma protein did not last long and so increase in osmotic pressure was of short duration A daily dose of 50 gm of salt poor albumin in 500 cc of water along with 30 gm of glucose produces considerable diuresis in the edematous patient The high cost of this human albumin and the relatively small available supply of it are factors limiting its therapeutic use

In place of purified human salt poor albumin transfusions of *human blood* and of *redissolved human dried plasma* have been used but they have not been as effective as the albumin probably because of their high salt content which is 7 times that of the salt poor human albumin

Instead of human albumin blood or redissolved dried plasma *acacia* has been used as a replacement substitute because it has a molecular weight similar to that of albumin and because it remains for some time in the circulation it causes an increase in osmotic pressure and brings about a diuresis Acacia has been purified so that it can be injected with only a moderate or no reaction It is to be used in a total dose of 90 gm as a 6 per cent solution of pure acacia in 1500 cc of 0 06 per cent solution of sodium chloride one third of this is to be given in each of 3 intravenous injections administered on alternate days Excellent clinical results have been reported following such use of acacia even considerably larger amounts have been used Some however oppose its use on the basis of continued presence of acacia in liver spleen and other body cells

Globin from human erythrocytes has also been used with the claim of excellent results A daily intravenous dose of 60 gm as a 4 per cent solution in normal saline repeated 6 times has been advised It is in expensive, being prepared from erythrocytes left over from the prepara tion of plasma which in turn can also be used in treating these patients as described in an earlier paragraph

Dextran a macromolecule composed of many units of dextrose has been used with some success in relieving edema It seems to have few side effects and when given repeatedly as a 6 per cent solution in a dose of 300 to 700 cc in 0 9 per cent saline solution is effective in re ducing edema Anaphylactoid reactions do occur and in studies on dogs large amounts of dextran caused focal degenerative lesions in the liver and kidney No abnormalities were observed, however, in humans who were carefully studied several months after receiving therapeutic amounts of dextran

Polyvinyl pyrrolidone (Kollidon) a synthetic compound made from acetylene, is being studied intensively and may be shown to have a useful role in the treatment of edema resulting from kidney disease Early results are promising but the product is not yet available for gen eral use

Gelatin, as a 6 per cent solution, given in a total daily dose of 50 gm, apparently is not toxic when given for short periods of time and oc casionally it may give good results

Methyl cellulose, like acacia has been generally abandoned because of the large amounts of it which are deposited in the liver

There has not yet been sufficient experience with pectin to determine its usefulness The long retention of the substance in the body, the oc currence of purpuric rashes, and its instability in alkaline solution make its widespread value in the treatment of edema very doubtful

Diuretic Drugs Since these various methods for increasing the os motic pressure of the circulating blood are not thoroughly satisfactory, and some are very expensive the removal of the excess edema fluid by the use of diuretic drugs is preferable Of these the *mercurial diuretics* are the most effective Those now available have a low toxicity and can be given safely, with the expectation of a considerable and prompt diuresis to either hospitalized or ambulatory patients with the edematous type of Bright s disease These mercurials are dispensed in sterile ampules as a 10 per cent solution of the drug The average dosage of a mercurial diuretic is 2 cc of a 10 per cent solution, given for most of the mer

substances and an eventual azotemia that will be lethal On the fortunate side are the facts that the healing process occurs fairly often in this type of Bright s disease and that often there is a considerably long period of slight albuminuria and no renal edema before azotemia begins

To increase the plasma albumin level toward normal use the *diets high in protein* given above Unfortunately high protein feeding is only very moderately effective in elevating plasma albumin and so we need to resort to other procedures Of these the intravenous injection of *purified human albumin* would seem most likely to be effective Purified human albumin has been prepared and its intravenous use has been tried As first used its salt content was too high and so a *salt poor human albumin* was made available This can be given without any disturbing reactions if given slowly but it was found that continued daily injections would be needed since this albumin disappeared rapidly from the circulation and much of it was excreted into the urine when there was a renal lesion causing marked albuminuria Consequently an induced increase in plasma protein did not last long and so increase in osmotic pressure was of short duration A daily dose of 50 gm of salt poor albumin in 500 cc of water along with 30 gm of glucose produces considerable diuresis in the edematous patient The high cost of this human albumin and the relatively small available supply of it are factors limiting its therapeutic use

In place of purified human salt poor albumin transfusions of *human blood* and of *redissolved human dried plasma* have been used but they have not been as effective as the albumin probably because of their high salt content which is 7 times that of the salt poor human albumin

Instead of human albumin blood or redissolved dried plasma *acacia* has been used as a replacement substitute because it has a molecular weight similar to that of albumin and because it remains for some time in the circulation it causes an increase in osmotic pressure and brings about a diuresis Acacia has been purified so that it can be injected with only a moderate or no reaction It is to be used in a total dose of 90 gm as a 6 per cent solution of pure acacia in 1500 cc of 0 06 per cent solution of sodium chloride one third of this is to be given in each of 3 *intravenous injections administered on alternate days* Excellent clinical results have been reported following such use of acacia even considerably larger amounts have been used Some however oppose its use on the basis of continued presence of acacia in liver spleen and other body cells

tube, when inserted through the skin on top of the foot or lower leg, will remove much edema fluid Even without an antibiotic local infection is rare If it occurs, it can be easily controlled with the antibiotic effective against the infecting organism

In a rare case potassium or calcium depletion occurs This should be recognized and treated by prompt replacement therapy

Thyroid Extract This once advised, should no longer be used as a method of treating the edematous type of Bright's disease

Treatment of Anemia Although these patients look very pale by reason of their edema, actually by blood examination anemia is infrequent and, if present, suggests some cause other than the Bright's disease, this cause should be sought out and treated accordingly For mild degrees of anemia ferrous sulfate or ferrous gluconate, 0 3 gm should be given 3 times daily after meals so long as anemia persists For more severe anemia transfusion of blood is advisable, followed by iron as just described and/or liver extract or vitamin B_{12} as described for Pernicious Anemia

Antibiotics If there is any evidence of an existing infection, penicillin or other antibiotic effective against the infecting organism should be given promptly in adequate dosage as described under their respective headings

Corticotropin and Cortisone The indications and contraindications for the use of these hormones in edematous Bright's disease are not yet clearly defined In the nephrotic syndrome particularly, they may have usefulness in causing temporary remission by diuresis sometimes a decrease or even disappearance of hyperlipemia and proteinuria and a restoration toward normal of serum protein levels Complications of treatment are common however, with hyperadrenocorticism occurring with prolonged administration In most instances the ultimate course of the nephrotic syndrome seems not to be much influenced by their use In chronic nephritis the use of corticotropin and cortisone is not recommended

Subacute and Chronic Hemorrhagic Bright's Disease

Prolonged bed rest is indicated, it should end when by trial of increased physical activity it is shown to have been ineffective Then somewhat restricted physical activity should be instituted The *diet*

curials either intravenously or intramuscularly for some subcutaneously on every second or third day or once a week as seems needed to keep the edema under control For the sake of safety the intramuscular route is recommended It is well to give first a test dose of 0 5 cc to detect any idiosyncrasy In some patients 1 cc will suffice while other patients *need from cc up to 4 cc Occasionally with continued use an increase* in dosage may be needed to obtain satisfactory diuresis a certain degree of habituation to these drugs seems to occur at times For intravenous or intramuscular use meralluride sodium solution (Mercuhydrin) mercurophylline injection (Mercuzanthin) and mersalyl and theophylline injection (Salyrgan Theophylline) seem at present to be satisfactory with a minimum of toxicity Mercaptomerin sodium [Thiomerin Sodium] is recommended for subcutaneous dosage this can be used also intravenously or intramuscularly when the subcutaneous route for any reason gives unsatisfactory diuresis With mercaptomerin the patient can be taught to give to himself the prescribed subcutaneous injections just as is done for insulin This obviously is a distinct advantage

Prolonged and excessive diuresis produced by mercurial diuretics may cause very great sodium depletion and this may be very deleterious to *the patient The development of a low salt syndrome can be recognized* by the appearance of the following phenomena (1) successive depression of the volume of the urine during 3 to 5 days (2) a depression of urinary chlorides to negligible quantities not increased by the giving of a mercurial diuretic (3) a rapid progressive gain in body weight (4) occasionally an increase in heart rate (5) an increase in non protein nitrogen in the blood (6) a fall in plasma levels of chloride and sodium and (7) such symptoms as (a) weakness drowsiness and lethargy (b) loss of appetite sometimes with thirst (c) nausea and occasional vomiting (d) occasional abdominal or muscular cramps and (e) a demonstrable increase in body fluids When salt depletion is evidenced by the developments just enumerated body sodium and chloride must be brought to normal levels promptly by slowly given intravenous injections of hypertonic (5 or 6 per cent) solution of sodium chloride When sodium depletion is not very great sodium chloride can be given by mouth or it may be given by mouth in addition to or following its intravenous use With increased intake of sodium and chloride diuresis usually ensues and non protein nitrogen levels in the blood drop toward normal values

If for any reason mercurial diuretics are not satisfactory a Southey

and this is unusual Overeating is even worse than indulgence in alcohol and should be stopped, more individuals overeat than overdrink or oversmoke

The food eaten should make up a diet — balanced in protein fat and carbohydrate with adequate content of vitamins — with the total calorie value such that the patient of average weight neither loses nor gains in weight, while the overweight patient has such reduction of carbohydrates and fats that he slowly loses weight down to a normal level Fluid intake should be neither small nor larger, the amount needed to maintain a 24-hour urine output of 1200 to 1800 cc, the patient's sense of thirst is usually a safe guide, and fluids need not be measured Moderation in the use of sodium chloride is desirable but it need not be greatly restricted

The 75 gm protein diet may serve as a guide in preparing a diet for these patients with non edematous Bright's disease

If the patient develops edema with very rare exceptions it is caused by a complicating cardiac insufficiency When this appears, it should be treated as described in the section on Treatment of Chronic Heart Disease

Climate and Exercise The ideal climate is a place with a minimum of extremes of temperature and moisture so that the patient can be free to be out of-doors often resting or taking a moderate amount of exercise With carefulness, however, the patient can live in any part of the United States and by and large does best in the climate to which he is accustomed where he can carry on his usual activities, including his occupation Until the disease is advanced and demonstrably crippling stopping work is not desirable, although moderation in carrying it on must be learned Most patients do not need to go away to a better climate in order to avoid upper respiratory infections It is to be remembered that the incidence of the common cold and of bronchitis and pneumonia is essentially the same in all parts of the United States including climatic resorts Moderate exercise, adapted to the individual's strength customs of activity and temperament, is desirable This should be planned by the patient's physician The patient should make periodic visits to his physician, at which time the *most important* thing is for the physician to learn in detail of the patient's activities and his reaction to them, how he spends his time, and what his pleasures and his antipathies are Laboratory tests blood pressure readings and physical examination should not be continuously *neglected, but they* should be the

should contain not less than 75 gm protein as described for Chronic Non edematous Bright s Disease Numerous treatments such as the administration of ergot administration of calcium transfusion of blood vaccines, tonsillectomy — even renal decapsulation — have been tried with the idea of stopping the renal bleeding none of them seems to avail

Chronic Non edematous Bright s Disease Chronic Vascular Nephritis Chronic Interstitial Nephritis

The treatment of this type of Bright s disease is the same whether it is the end stage of an unhealed acute Bright s disease progressing into chronic disease with dominatingly glomerular lesions the end stage of the edematous type of Bright s disease the end or healed stage of pyelonephritis a progressing vascular lesion often associated with hypertension or a form of vascular nephritis commencing insidiously without any of the just mentioned antecedents These various clinical types of chronic non edematous Bright s disease have as a common denominator a kidney smaller than normal in size with an increased amount of interstitial fibrous tissue and glomeruli and tubules showing *sclerosing and degenerative lesions a kidney which functions with a* decreasing efficiency that leads to increasing retention within the body of those substances except water normally excreted by the kidney Treatment is then to be directed toward retarding progression of the lesions preventing and controlling exacerbations and adapting body *metabolism to the decrease in the excretory activity of the kidney*

Treatment to these ends is in large part a matter of regulating general hygiene with a view to reducing to a minimum the incidence of infections and infectious diseases treating them as promptly and effectively as possible including the use of appropriate antibiotics and providing functional rest to the kidney and physical and mental relaxation to the patient Early recognition of the condition helps in guarding the patient against infections and infectious diseases and in preventing excesses in eating drinking and various activities of life We know of no therapeutic measures that will directly influence the pathological lesions in the kidney

Diet Strong alcoholic drinks are best interdicted Light wines in moderation do no harm Moderate use of tobacco may be continued *unless the individual has some unpleasant or untoward reaction from it*

0 3 gm, should be given 3 times a day over long periods of time Cobaltous chloride is usually of little or no value in treating this type of anemia In an occasional case however, it is helpful A dose of 50 to 100 mg given as a 2 5 per cent solution after meals is recommended Patients who are receiving this drug must be closely observed, since serious gastro-intestinal reactions and other toxic symptoms may occur

Lower Nephron Nephrosis

This type of renal lesion with its numerous causes should have essentially the same treatment, whatever its cause, except that in the form following crush injuries transfusion of incompatible blood, and various forms of hemolysis of the blood there is the additional need of removing from the circulation the heme pigments which have been formed and which are factors in causing the anuria of lower nephron nephrosis When the presence of heme pigments is not great, the use of the artificial kidney or transperitoneal drainage and other methods described for the treatment of Uremia should be used When heme pigment is a significant causative factor of the anuria, extensive bleeding followed by replacement transfusion of fresh blood should be used and repeated several times with or without the use of the methods referred to in the preceding sentence

It is very important in these patients not to use diuretic drugs and not to force fluid Mercurial diuretics cannot be expected to cause diuresis in these patients, and they will further damage the cells of the lower nephron If fluid intake is not restricted, pulmonary edema is apt to occur and introduce a serious problem for treatment In these patients if life can be preserved anuria, as a rule, ends between the seventh and twelfth day, life with subsequently few aftereffects is compatible with anuria of this duration and sometimes for more than this number of days Knowing this, it is important not to overtreat patients with lower nephron nephrosis

During the anuric phase only enough fluid should be given to replace fluid excreted plus 1000 cc for insensible and other losses, with careful regulation of electrolyte balance During the period of diuresis fluid loss should be replaced carefully for excess even volume for volume can overload the circulation with resulting pulmonary edema Electrolyte balance remains all important, particularly of calcium and potassium

least important part of the consultation If and when any unusual symptoms appear or if there is evidence of an infection the patient s physician should be called or visited in his office The patient has a disease which he must learn to live with because it cannot be cured

Focal and Other Infections and Infectious Diseases These when present should be treated promptly and thoroughly by modern methods as described elsewhere in this book Actual focal infections should be treated including removal of diseased tonsils and teeth provided there is adequate evidence that potentially or actually they are doing harm Fortunately overemphasis on removing so called focal infections has very largely disappeared In the past, all too often tonsillectomies dental extractions and sinus drainages bespoke an unfounded belief in their causal relation to many chronic ills

Treatment of Special Conditions Uremia should be anticipated by following the phenolphthalein excretion and blood level of urea or non protein nitrogen When the former decreases to only a small amount and the latter definitely increases then a diet low in protein such as the 26 gm protein diet with low salt content should be given unless salt depletion is present when the latter occurs additional sodium chloride should be given Also fluid intake should be increased provided this causes an increase in excretion of urine this is particularly important when there are signs of dehydration Then it is often advisable to give fluid intravenously in the form of 5 per cent glucose in normal saline solution These methods often avert definite uremia If nausea and vomiting develop or if any of the symptoms of uremia appear then treatment should follow along the lines already described under Acute (Hemorrhagic) Bright s Disease

Restlessness muscle twitching and *convulsions* should be treated as already described

Headache often a very troublesome symptom in this type of Bright s disease both with and without accompanying hypertension should be treated as described under Headache while the methods already indicated for uremia are also carried out

Pruritus is not infrequent and may be very annoying It should be treated as described for pruritus accompanying jaundice

Anemia is very usual as renal insufficiency increases in patients with chronic non edematous Bright s disease Often repeated transfusions of blood are very helpful and should be given whenever the anemia is of considerable degree When less marked ferrous gluconate 0 2 to

Amyloidosis of Kidney Myeloma Kidney Sarcoidosis of Kidney These conditions often present, so far as renal function is concerned, the clinical picture of some form of Bright s disease, usually the chronic type but occasionally the acute Treatment should be that already described in the preceding pages for the form of Bright's disease whose clinical picture is shown In addition there should be treatment as de scribed elsewhere for amyloid myeloma, and sarcoidosis Sarcoidosis sometimes clears up spontaneously

Polycystic Kidney Renal Agenesis Hypoplasia These lesions of the kidney present the clinical picture of chronic non edematous Bright s disease and should have treatment appropriate to that condition In polycystic kidney the infection of cysts is not infrequent, and requires the use of antibiotics and possibly surgical drainage Sometimes pyelitis or pyelonephritis co exists if so, treatment should be as described for these conditions

Renal Cysts Often these, from infection or from their bulk, will need surgical drainage and/or excision If infected, an antibiotic may be effective, but this is not probable unless surgical drainage is also applied

Renal Tuberculosis This often requires surgical treatment along with the usual general and specific measures used in treating tuberculosis elsewhere in the body As a rule in these cases, tuberculosis also exists in body tissues other than renal

Syphilis of Kidney This is unusual Treatment should be as described for Syphilis

Tumors of Kidney These usually require nephrectomy but occa sionally simple excision is sufficient

Special Forms of Renal Disease

Kimmelstiel Wilson syndrome is usually a combination of diabetes mellitus hypertension and edematous type of Bright s disease and in treatment involves the use of methods described for the management of diabetes mellitus those for the management of hypertension and its complicating cardiac decompensation if that is present and those for the management of edematous type of Bright s disease Since in many of the patients with this syndrome there develops sooner or later a varying degree of azotemia it is important to make determinations at fairly frequent intervals of blood urea or non protein nitrogen and to plan the protein content of the diet on the basis of these findings de creasing the protein as urea or non protein nitrogen figures increase This is important because before this happens most of these patients will be getting a diet with high protein content

Cortical and/or Papillary Necrosis of the Kidney Since in these con ditions particularly in papillary necrosis bacterial infection is present the patients should be given an antibiotic selected on the basis of the susceptibility of the infecting bacterium found in cultures from the urine in most cases penicillin If the lesion is unilateral nephrectomy may be the treatment of choice For these patients the methods appro- priate to the treatment of lower nephron nephrosis are to be used

Traumatic Uremia Crush Syndrome Myoglobinuria Hemoglo binuria Blackwater Fever Transfusion Renal Reactions Hepatorenal Syndrome These are a variety of diagnostic terms used for a type of renal lesion which in general has the characteristics of lower nephron nephrosis and should be treated as described for that condition

Sulfonamide Kidney In its simple form this is hematuria and follows the therapeutic use of one of the sulfonamides as a rule when detected early as it should be by making frequent examinations of the urine for the presence of red blood cells the only treatment necessary is to stop the use of the causative sulfonamide to increase fluid intake and to alkalize the urine by giving sodium bicarbonate in needed amount

If urine excretion decreases and crystals of the sulfonamide are found in the urine ureteral catheterization with flushing out of the renal pelvis with normal saline solution is indicated in addition to the methods described in the preceding paragraph

If these methods fail to start a diuresis or if anuria appears the treat ment described for lower nephron nephrosis should be used

of the urine is needed since a concentrated highly acid or alkaline urine is in itself irritating to and a source of discomfort in the urinary tract A 24 hour urine output of 3000 cc or even more should be obtained if possible To that end each patient should be given 3000 to 4000 cc of fluid daily at and between meals In addition to water various carbonated drinks like ginger ale, various flavored non alcoholic drinks, fruit juices milk and hot or iced coffee and tea should be used to give variety and to make possible a continued daily intake so that the 24 hour urine output will be at least 2500 cc, preferably more

Various symptoms such as headache, nausea, vomiting diarrhea or constipation will need symptomatic treatment, and this should be given as described in Chapter 1

Urinary Antiseptics Some one of these should be given promptly to all of these patients with the exception of the occasional very mild case which will clear up on bed rest and increased fluid intake As soon as possible the infecting organism should be identified for effective antisepsis will depend on the use of that antiseptic known to be active against the causative bacterium, it is far more efficient to know rather than surmise what the organism is In the majority of these cases however, there is usually time to try out a urinary antiseptic, so it is wise to use one that costs relatively little first rather than a costly one, and thus find out whether or not the cheaper one will be effective If it is not, then another more expensive one can be tried There is a great deal of difference in the relative cost of different urinary antiseptics, as shown by a recent drugstore inquiry for example an ordinary day's treatment with aureomycin costs 20 times more than one with sulfisoxazol (Gantrisin) or sulfadiazine Often simple inexpensive therapy will give satisfactory results in inflammatory conditions in the urinary tract

In milder infections of the urinary tract methenamine mandelate (Mandelamine) should be used It is effective only in acid urine preferably with a pH of 5 5 or one of greater acidity The drug usually creates a sufficiently acid urine for effective action unless urea splitting bacteria are present In that case, acidifying agents such as sodium biphosphate, 1 to 2 gm, or ammonium chloride, 2 gm, 3 times a day are needed A dose of 1 0 gm of methenamine mandelate 3 times a day is usually sufficient In general excellent results are obtained in the common urinary tract infections

In more severe infections and in those not responding to methenamine mandelate a sulfonamide or antibiotic should be utilized Sulfisoxazol

CHAPTER L

DISEASES OF THE KIDNEY AND URINARY TRACT

CYSTITIS URETERITIS PYELITIS PYELONEPHRITIS PYONEPHROSIS RENAL ABSCESS PERINEPHRIC INFLAMMATION

These inflammatory conditions of the urinary tract which usually occur in combinations rather than singly, need essentially the same plan of treatment consisting of certain general measures urinary anti septics and surgical procedures the latter if there is obstruction to the flow of urine at any point

General Measures Except in very mild cases bed rest is an essential in treatment The patient should lie flat in bed and when the inflammatory condition involves the ureter or renal pelvis a firm pillow should be placed under the loins to facilitate renal flow at these points The diet should be a simple nutritious one complete in protein fat carbohydrate and vitamins with its components selected to accord with the patient s preferences and to furnish high calorie value If the patient is obese fat forming foods should be restricted or omitted Except for this and the avoidance of highly seasoned and spiced foods and condiments there is no need for any prohibitions of particular foods so far as effect on inflammatory disease of the urinary tract is concerned With high fever frequent sponging of the patient is indicated particularly when there is much sweating The patient s back especially the bony prominences should be guarded against prolonged pressure and protecting rings should be used at once if any evidence of pressure lesions to the skin appear By keeping the back sedulously clean and dry and well powdered after alcohol rubs decubitus will be prevented Here preventive care will remove the need for actual treatment of pressure lesions

A large fluid intake however is very important in the treatment of these patients because a free flow of urine is needed to act both as a diluent of the urine and as a flushing or drainage mechanism Dilution

These should be tested against the infecting bacteria and the most effective combination used With some one of the antibiotics, selected as just discussed it will be possible to treat inflammation of the urinary tract effectively unless there is obstruction at some point to flow of urine or unless calculi are present Under these circumstances surgical procedures are indicated

All too frequently the presence of a few bacteria and a few pus cells in the urine is ignored, with the result that an infection in the kidneys goes on slowly and relentlessly, eventually causing death of the patient in uremia from chronic pyelonephritis Any infection of the urinary tract should be treated promptly and thoroughly toward its eradication Furthermore also too frequently, a few days of treatment are considered sufficient only to have the infection recur from time to time A prolonged schedule of treatment should be outlined, in terms of 4 to 6 weeks instead of days for patients with urinary tract infection to obtain the best results and to prevent the end picture of pyelonephritis

Surgical Procedures In all infections of the urinary tract and certainly in those cases proving resistant to methods of treatment described in the paragraphs above early instrumental exploration and x-ray study, with a radio-opaque substance, are to be carried out Often renal calculi are present to obstruct renal outflow or, as foreign bodies, prevent a sulfonamide or antibiotic from sterilizing the urine Such calculi should be removed surgically

In inflammation of any muscular tube, interference with its peristaltic activity is probable and actual obstruction is frequent If these occur instrumental dilatation and drainage are indicated to restore free flow of urine possibly in some cases other forms of surgery will be needed in particular prostatectomy After restoration of normal urine flow by surgical procedures more successful sterilization of the urine will be possible and the patient s condition can be cured or at least greatly ameliorated so that a reasonably comfortable life is possible

In certain patients not responding to the therapeutic methods already described particularly those with pyelonephritis most marked on one side unilateral nephrectomy or nephrostomy will be needed These operations may be used too in those cases in which renal function is nearly nil on one side and fair on the other the kidney with better renal function being left untouched When the lesion is bilateral with very poor excretory function of both kidneys, nephrectomy will be contraindicated and only some amelioration can be expected from general

(Gantrisin) in an initial mouth dosage of 4 gm followed by 2 gm daily should be tried It has a low toxicity and does not tend to cause a disturbing crystalluria Sulfadimetine (Elkosin) like sulfisoxazol is highly soluble in the urine and does not tend to cause crystalluria It is also effective and is given in the same dose Sulfadiazine in the same dosage may be substituted for sulfisoxazol or sulfadimetine in cases where these are not satisfactorily effective With the use of sulfadiazine it is wise to keep the urine alkaline by giving sufficient sodium bicarbonate to prevent or at least greatly decrease crystalluria and incidental hematuria Some prefer to use a combination of two sulfonamides such as sulfathiazole and sulfadiazine since it has been observed that with two sulfonamides a smaller total dosage is effective and toxicity and crystalluria are less These combinations make the possibility of a sensitivity reaction more likely, however and add little to therapy Their use is being replaced by sulfisoxazol and sulfadimetine Patients with chronic pyelonephritis who have considerable renal damage and are secreting a continually alkaline urine can frequently be carried along with considerable success on small doses of sulfisoxazol or sulfadimetine usually 1 0 to 2 0 gm a day for long periods of time These antibacterials prevent secondary bacterial invasion and not infrequently control the chronic infection while at the same time there is little danger of their causing renal damage

At present however an antibiotic seems preferable to a sulfonamide in the treatment of inflammations of the urinary tract antibiotics are more effective are free of the disadvantage of producing a crystalluria and have less propensity to any important toxic manifestations If the infecting organisms are streptococci or staphylococci procaine penicillin in aqueous suspension in a daily dose of 300 000 to 600 000 units given intramuscularly will be effective except in the presence of some strains of *Streptococcus fecalis* and *Staphylococcus aureus* and *albus*, which in test will prove resistant to penicillin If penicillin is ineffective streptomycin in a dose of 1 0 to o gm daily intramuscularly will often give gratifying results against many urinary tract invaders Of more constant effectiveness as a urinary antiseptic is aureomycin by mouth in a dosage of 250 to 500 mg 4 times daily Aureomycin has the double advantage of effectiveness against almost all of the bacterial flora of the urinary tract and of not needing a parenteral route of dosage Unfortunately it is still a costly drug If aureomycin does not prove effective it should be combined with sulfisoxazol (Gantrisin) sulfadimetine (Elkosin) or some other antibiotic such as streptomycin chloramphenicol or terramycin

salicyclic acid and Isonicotinic Acid Hydrazide for the treatment of pulmonary tuberculosis. See also pages 142-3.

Since tuberculosis of the urinary tract is very often complicated by inflammation caused by bacteria other than tubercle bacilli, antibiotics effective against them should be used. With tuberculous lesions present in the bladder, local treatment of focal lesions should be carried out through the cystoscope, even though there is evidence of tuberculous lesions high up in the urinary tract. A thorough trial of rest and antibiotic therapy should be made. If the urinary tract lesions are progressing, surgical measures may be helpful.

If the tuberculous lesion is extensive in the kidney, particularly when the involvement is dominantly unilateral, the tuberculous kidney should be removed, even if there are also tuberculous lesions at lower levels of the urinary tract, often the latter improve following unilateral nephrectomy. Nephrectomy is especially indicated when one kidney with tuberculous lesions has a very low degree of function. Many recommend removal of one kidney, the one with the worst renal function, when the tuberculous lesion is bilateral, since improvement in the condition of the less involved kidney has been observed to follow removal of the one most involved. In some patients study will show that one kidney has been almost destroyed by tuberculosis and that its function is almost nil, it is obvious that such a kidney should be removed unless total renal function is so low that any operation is contraindicated.

Calculi often complicate tuberculosis of the kidney or bladder. Their removal is usually a desirable part of the treatment of tuberculosis of the urinary tract.

The advice and services of a genito-urinary surgeon are a necessary adjunct to the study and treatment of tuberculosis of the urinary tract.

Hydronephrosis

Curative treatment of hydronephrosis will require skilled plastic surgery to remove or side track the block to urine flow at the pelvo ureteral juncture unless the hydronephrosis is caused by a calculus. Then removal of the calculus would be the procedure of choice, possibly plastic surgery, too would be necessary. If the hydronephrosis has been of long standing and very marked so that renal function of one kidney has become extremely slight unilateral nephrectomy should be carried out. If with hydronephrosis there has been infection, the treatment

measures and the use of urinary antiseptics In certain of these last mentioned cases some advise trial of nephrostomy on the side where renal function is better

If pyonephrosis perirenal infection or intranephric or perinephric abscess can be diagnosed then after a trial of large doses of an antibiotic has failed to cure surgical drainage and possibly nephrectomy are in dicated and should be carried out the findings at the time of exposing the kidney will determine just what the surgeon should do

If cystitis is the only or the main form of inflammation catheterization with emptying and washing out the bladder using a mildly antiseptic solution will often be an effective addition to the general plan of treatment outlined in the preceding paragraphs If there is an element of prostatic obstruction catheterization may be needed and repetition at frequent intervals will probably be necessary until the prostatic obstruc tion can be relieved by a surgical procedure

In some of these patients improvement is retarded by focal ulcerative or proliferative lesions in the bladder Cystoscopy will be needed to show these If such are found they should be treated by local applications or possibly by fulguration through the cystoscope

The physician will be wise to seek help from the genito urinary surgeon for every patient with pyuria and other symptoms persisting after a week or 10 days during which time the application of the recom mended general measures and urinary antisepsis has failed to cure the condition

Tuberculosis of the Urinary Tract

When there is a tuberculous lesion localized at any point in the urinary tract the patient should be treated with all of the general measures already recommended for tuberculosis In addition for the tuberculous process localized in the urinary tract much of the treatment described for Cystitis Ureteritis Pyelitis et cetera should be applied

At present the only antibiotic with any restricting effect on the activity of tubercle bacilli is streptomycin Although results from its use are not completely satisfactory it would seem wise to give it a trial An intramuscular dose of 1 to 2 gm every other day for a long period is recommended to be stopped if toxic symptoms especially vertigo tinnitus or deafness develop It should be combined with para amino-

The use of acetylsalicylic acid or salicylamide to increase urinary glucuronide excretion seems to prevent the recurrence of calcium containing stones since calcium phosphate solubility is enhanced by glucuronide A daily dose of 2 0 gm of either substance, divided and given in four equal doses, is recommended Treatment should be for long periods of time or until the tendency for urinary calculi has ceased

As already stated, the possibility of a causative parathyroid neoplasm or hyperplasia should be thought of, especially with recurrent nephrolithiasis, and this possibility should be eliminated by using the Sulkowitch test on the urine, this test consists of adding to an equal part of urine a solution composed of 2 5 gm each of oxalic acid and ammonium oxalate and 5 cc of glacial acetic acid in 150 cc of distilled water When this causes no precipitate, there is no calcium in the urine, while if there is a fine white cloud the serum calcium concentration is probably within normal limits, and the parathyroids are not causative of the nephrolithiasis A dense milky precipitate indicates hypercalcemia and probably neoplasm or hyperplasia of the parathyroids, which should be treated as the important feature of the management of this type of nephrolithiasis

If the patient has gout, nephrolithiasis is more liable to occur Gout should be treated adequately as part of prophylaxis against nephrolithiasis If nephritis is present it is usually of the vascular type

Neoplasm of the Urinary Tract

Neoplasms of the urinary tract, if malignant or if causing symptoms, should be removed as soon and as thoroughly as possible This is a surgical condition, not a medical one, and patients with probable neoplasm of the urinary tract should be transferred promptly to a competent surgeon

BIBLIOGRAPHY

1 ADDIS T *Glomerular Nephritis Diagnosis and Treatment*, Macmillan Co N Y, 1948
2 BRADLEY, S Management of the Patient with Chronic Diffuse Glomerulonephritis' *Med Clin No Amer*, Sept 1945 p 1184
3 CHRISTIAN, H A *Bright's Disease*, Oxford University Press N Y 1948

described for pyelitis and pyelonephritis would be in order If hydronephrosis is bilateral and marked drainage by fistula through the loin region would be the only probably effective treatment with the possibility of later plastic surgery and subsequent closure of the fistula

Nephrolithiasis

Recurrent nephrolithiasis may be caused by parathyroid neoplasm or hyperplasia if so its treatment should be the removal of the abnormal parathyroid tissue If the cause is an inflammation of the urinary tract with obstruction this should be treated thoroughly With this treatment and correction of obstruction if present small calculi may be passed large calculi will require instrumental or operative removal and it will be wise not to delay removal of calculi too large to be passed without instrumentation of some sort Patients with renal calculi should have their renal function tested prior to continued treatment or surgical removal A large fluid intake should be part of continued treatment

For an attack of renal colic relief should be given as promptly as possible for renal colic is about the worst pain man is heir to When the pain is intense morphine sulfate 15 mg with atropine sulfate 0 5 mg should be given hypodermically to be repeated in 15 minutes and several times later if pain is not relieved or if it recurs It is also advisable to give with or just after the first dose of morphine an intravenous injection of 10 cc of 10 per cent calcium chloride or 20 cc of 10 per cent calcium gluconate which should be repeated in 1 hour if pain continues to be unrelieved Amyl nitrite inhalation is of some help and should be given while other measures are being prepared Aminophylline 0 5 gm intravenously should also be tried for colic

A hot bath will often help relieve the pain care must be taken to see that the water is not so hot that it will burn the patient a danger which is often real because with his intense pain the patient is not so sensitive to heat

In prophylaxis a large fluid intake is needed and the urine should be kept acid by frequent doses of enteric coated tablets of ammonium chloride unless the calculi are uratic in which case an alkaline urine is needed If there is oxaluria or if an oxalate calculus has been passed such foods as tea coffee cocoa pepper rhubarb spinach beetroot beans tomatoes strawberries cranberries radishes grapes currants and figs should be avoided or taken only in small quantity and infrequently

4 ELKINTON J R CLARK, J K SQUIRES R D BLUEMLE, L W and CROSLEY A P Treatment of Potassium Retention in Anuria with Cation Exchange Resins Preliminary Report *Am Jour Med Sc*, 1950 ccxx p 547

5 KIMMELSTIEL P and PORTER W B 'Intercapillary Glomerulosclerosis *N E J Med*, 1948 ccxxxviii pp 876 908

6 LUETSCHER J A Jr and DEMING Q B Treatment of Nephrosis with Cortisone *J Clin Invest* 1950 xxix p 1576

7 MERRILL J P SMITH S III CALLAHAN E J III and THORN G W Use of the Artificial Kidney Clinical Experience *J Clin Invest* 1950 xxix p 425

8 RAPOPORT M McCRORY W M BARBERO G BARNETT H S FORMAN C W and McNAMARA H Effect of Corticotropin (ACTH) on Children with the Nephrotic Syndrome *Jour Amer Med Assoc*, 1951 cxlviii p 1101

9 RAVIN I S ARONSON P R and YULES J H Complications of the Diuretic Phase of Lower Nephron Nephrosis *N E J Med* 1951 ccxlv p 830

10 THORN G W Treatment of Renal Insufficiency *Jour Urol* 1948 lix p 119

11 THORN G W MERRILL J P SMITH S III ROCHE M and FRAWLEY T F Clinical Studies with ACTH and Cortisone in Renal Disease *Arch Int Med* 1950 lxxxvi p 319

12 WALLENIUS G Relief of Nephrotic Edema by Dextran Infusions *Scand J Clin and Lab Invest*, 1950 ii p 228

13 WHITEHILL M R LONGCOPE, W T and WILLIAMS R The Occurrence and Significance of Myocardial Failure in Acute Hemorrhagic Nephritis *Bull Johns Hopkins Hosp*, 1939 lxiv p 83

14 WEISS S and PARKER F JR Pyelonephritis Its Relation to Vascular Lesions and to Arterial Hypertension *Medicine*, 1939 xviii p 221

15 BIRCHALL R and ALEXANDER J E Medical Aspects of Pyelonephritis *Medicine* 1950 xxix p 1

16 PRIEN E L and WALKER B S Salicylamide and Acetylsalicylic Acid in Recurrent Urolithiasis *Jour Amer Med Assoc* 1956 clx 373

17 LUETSCHER J A Jr DEMING A B JOHNSON B B and PIEL C F Advances in Management of the Nephrotic State *Jour Amer Med Assoc* 1953 cliii 1236

18 OLIVE, J T Jr MILLS S T and LUNDY J S Dextran for Nephrotic Edema *Proc Staff Meet* Mayo Clinic, 1953 xxvii 199

most helpful, especially in the presence of pain Fluids in abundance should be given by mouth, if the patient tolerates them Oxygen inhalations are indicated, if there is dyspnea, air hunger, or any degree of cyanosis Normal body temperature is maintained by application of sufficient heat in the form of warm blankets, hot-water bottles, and hot drinks Excessive heat may be harmful

Transfusion is indicated if cyanosis dyspnea, air hunger, rapid pulse fall in blood pressure severe pallor or sweating appears Whole blood is much to be preferred and after careful cross matching including check of Rh factors 500 to 750 cc should be given and repeated as the clinical condition of the patient indicates Whenever possible, blood of the same type as the patient s should be used This is particularly important if there is a possibility of repeated transfusions

If whole blood is not readily available, transfusion of 500 to 1000 cc of plasma and 1000 cc of 5 or 10 per cent glucose solution or normal saline may be substituted until whole blood can be obtained If fluids are not tolerated by mouth sufficient normal saline is to be given intravenously to correct dehydration For patients in severe shock the polysaccharide (Dextran) given as a 6 per cent solution in a dose of 300 to 700 cc in a 0 9 per cent saline solution is helpful in maintaining blood pressure Polyvinyl pyrrolidine (Kollidon), given as a 3 5 per cent solution in normal saline or medicinal grade pectin (N F), 1 per cent in normal saline is also effective These agents, like Dextran, are not as useful as whole blood or plasma but they can be life saving until blood can be obtained

As soon as the acute phase is over patients should be given a nutritious diet high in vitamins protein and iron If by repeated blood counts, blood regeneration is found to be lagging, it may be stimulated by iron therapy Ferrous gluconate, 0 3 gm after meals is satisfactory

Chronic Blood Loss Chronic Hemorrhage

The cause of the bleeding must be sought for and corrected when possible A diet rich in protein vitamins and iron is to be given Bed rest or restriction of activities is indicated for the dyspneic or weak patient The pulse rate serves as an excellent guide to the degree of permissible activity Patients with severe anemia who are weak dyspneic have marked pallor or low blood pressure, benefit from transfusion of 500 to

PART XVI

DISEASES OF THE BLOOD

CHAPTER LI

DISEASES AFFECTING PRIMARILY THE ERYTHROCYTES

The many diseases affecting the blood may be arranged into 3 general groups They are diseases affecting the erythrocytes those affecting the leucocytes and those effecting several or all of the blood elements

Diseases that primarily affect the erythrocytes can be divided into those that decrease and those that increase the number of circulating cells

Those conditions causing a decrease in the number of circulating erythrocytes vary widely in their mode of action and the type of lesion produced but all result in an anemia Treatment is to be directed toward its amelioration Once the anemia is controlled most cases are relieved from associated pathological physiology

ACUTE BLOOD LOSS ACUTE HEMORRHAGE

Acute hemorrhage if sufficiently severe will produce shock lowering of the blood volume and severe anemia Treatment should consist of prompt control of the hemorrhage *prevention or management of shock restoration of blood volume and measures to relieve the anemia*

Until hemorrhage is well controlled patients must be kept resting quietly in bed preferably with the head lowered Apprehension restless ness or pain may be relieved by sedation Morphine sulfate 10 mg is

Chlorosis

This iron deficiency disease, now rarely seen responds promptly to the program outlined for chronic hypochromic anemia Hygienic corrective measures are to be stressed Adequate exercise, fresh air, sunshine, and a nutritious diet are recommended

Hypochromic Anemia of Pregnancy

This iron deficiency anemia responds readily to iron therapy Ferrous sulfate 0 3 gm or ferrous gluconate, 0 6 gm, each 3 times a day after meals, and a diet rich in meat, eggs, beans, beet greens, whole grain cereals, dried apricots and peaches quickly correct the anemia This hypochromic microcytic, true iron deficiency anemia should not be confused with the common anemia that develops during pregnancy, where the red blood cells are of normal size and contain normal amounts of hemoglobin The latter probably results from an absolute increase in plasma volume and is consequently "physiological" and does not require or respond to any therapy

Pernicious Anemia

Before therapy is initiated it is essential that an accurate diagnosis be established Bed rest and careful regulation of activities are recommended for those patients with severe neurological involvement or a marked anemia Bed rest should be continued until the erythrocytes are over 3 000 000 and resumption of activity should be graded to avoid fatigue Care must be taken with neurological cases to avoid injuries and overactivity The patient however, should not be confined too closely to bed If the erythrocyte count is 2 000,000 or less bed rest with limited activity is necessary As soon as strength permits coordination re education exercises may be commenced

A nutritious diet containing an abundance of meat and vitamins especially C and the B complex group is recommended It should be bland at first if the tongue and mucous membranes are inflamed or sensitive

Blood transfusions are of limited value and are indicated only as an emergency measure for the seriously ill patient with an extreme degree of anemia or for those with a seriously complicating disease In general

750 cc of whole blood secured from donors who should have the same blood group as the recipient whenever possible

Iron is of distinct value and ferrous sulfate 0 3 gm, or ferrous gluconate 0 6 gm by mouth 3 times a day after meals is excellent

Occasionally a daily oral dose of folic acid 10 mg or of liver extract 1 0 cc (15 units) or vitamin B_{12} 10 to 25 micrograms daily the latter given intramuscularly may facilitate recovery Usually however they are of little or no help

Iron Deficiency Chronic Hypochromic Anemia

This anemia responds readily when adequate amounts of iron are given once the causative factor is corrected The primary cause of the iron lack should be sought for and removed Many conditions can produce a hypochromic anemia diets low in iron poor absorption of iron such as occurs in severe diarrhea sprue pellagra hookworm and tapeworm infections severe infections of or damage to the gastro intestinal tract and surgical removal of large amounts of the absorbing intestine If any of these conditions exist they should be corrected promptly if possible Dietary education and hygienic instruction are often required Elimination of chronic infection is essential If achlorhydria or hypochlorhydria is present dilute hydrochloric acid U S P 2 to 4 cc mixed in half a glass of fruit juice and administered through a glass tube is helpful

A nutritious diet containing foods rich in iron such as beans eggs liver beef pork lamb broccoli leaves beet greens spinach whole grain cereals apricots and peaches is recommended Iron as ferrous sulfate 0 3 gm 3 times a day after meals or ferrous gluconate 0 6 gm given in the same manner is effective

Treatment should be continued until the hemoglobin and red blood cells have returned to and remain normal A therapeutic response as evidenced by an increase in the reticulocytes is usually present by the tenth day of treatment As a rule the hemoglobin rises at the rate of 0 1 to 0 3 gm per 100 cc per day if the patient is responding satisfactorily Once the normal values are obtained the dose of iron should be reduced Usually one third the original dose is sufficient To avoid relapse the administration of iron should be continued usually for several months If monthly checks continue to show normal values iron may be discontinued

time the dose should be reduced to 15 units every 2 or 3 weeks depending on the patient's needs Usually 1 U S P unit a day is sufficient for maintenance

Patients with neurological involvement should receive vitamin B_{12} 40 micrograms intramuscularly followed by 15 to 30 micrograms every 2 days for 3 months The same dose should then be given weekly for at least 1 year until neurological improvement is no longer apparent The dose is then reduced to 15 or 30 micrograms every 2 or 3 weeks If liver is preferred, the concentrated liver extract should be given intramuscularly in a dose of 15 units daily for 2 weeks followed by 15 units twice a week for 3 months and 15 units weekly thereafter as long as neurological improvement is apparent When neurological improvement is no longer evident, the dose may be reduced to 15 units every 2 weeks These patients must be observed carefully The erythrocytes should be maintained at 5 000,000 or better, if that is possible If the count falls below this or if there is evidence of neurological progression weekly or biweekly doses for a period of 3 to 6 months are recommended Some patients require weekly or biweekly doses to remain symptom free There need be no fear of producing polycythemia

Therapy must be continued through life Patients are advised to have blood examinations at 6 month intervals and should consult their physicians if any untoward symptoms of any sort arise Dosage should be increased in the presence of severe arteriosclerosis fever infections surgical operations or complicating disease

Normally response to vitamin B_{12} or liver extract is prompt in 3 to 4 days patients should notice improvement in appetite strength and sense of well-being often these appear before hematologic response is evident The hematologic response is characteristic Reticulocytosis usually reaches a peak in approximately 7 to 10 days Patients with 1 000 000 erythrocytes should exhibit a reticulocyte response of 30 per cent or more those with 2 000 000, a reticulocyte count of 15 per cent or more and those with 3 000 000 a response of not less than 4 per cent The rise in erythrocytes is the true measure of therapy the more severe the case, the greater this response to treatment As a rule weekly blood counts will show an increase in the red cells of from 30 000 to 100 000 a day A complete hematological remission with a return of hemoglobin and red blood cell count to normal values should be attained in approximately 8 to 10 weeks Neurological signs and symptoms are generally completely relieved or markedly improved under this plan of treatment

transfusions should be reserved for those with an erythrocyte count of 1,000 000 or less When available the use of the red cell residue left from plasma and albumin production resuspended in physiological saline is to be preferred since transfusion reactions are much less likely to occur following its use

Iron therapy is not usually indicated unless there is an associated iron deficiency anemia or a chronic bleeding lesion Patients requiring iron must be studied carefully and the cause of the complicating secondary anemia ascertained The relatively great incidence of carcinoma of the stomach in these patients must be borne in mind Female patients with pernicious anemia before the menopause are frequently benefited by the addition of iron therapy to their dosage of liver or Vitamin B_{12} When indicated iron may be given as ferrous sulfate 0 3 gm or as ferrous gluconate 0 6 gm both 3 times a day after meals

Hydrochloric acid occasionally affords symptomatic relief from the *dyspepsia and diarrhea that may be observed in pernicious anemia* patients It is to be given as the dilute hydrochloric acid U S P in a dose of 2 to 8 cc after meals 3 times a day well diluted in a half to full glass of water or fruit juice and administered through a glass tube in order to protect the teeth After remission has been induced the use of hydrochloric acid is warranted only in the rare patient who without it continues to have indigestion or diarrhea

Specific treatment with vitamin B_{12} or liver extract must be started promptly and continued without cessation Patients with anemia but without neurological complications should be given an initial dose of *40 micrograms of vitamin B_{12} intramuscularly followed by 15 to 30* micrograms 2 or 3 times a week for the next 4 weeks Following this 30 micrograms should be given every week until the blood cell count becomes and *remains normal The dose may then be reduced to 15 to 30* micrograms every 3 or 4 weeks Dosage must be individualized and adjusted to the needs of the patient Vitamin B_{12} does everything that liver extract will do and *is much less expensive It can be used for* patients allergic to liver Some physicians still prefer liver and feel that it increases appetite and gives perhaps better over all results For those desiring to use liver the concentrated liver extract should be given intramuscularly 1 cc equivalent to 15 U S P units daily for the first 10 days to 2 weeks 15 units 3 times a week for the next 4 weeks 15 units 2 times a week for the next month and then 15 units every week until the red blood cell count becomes and remains normal at which

therapy in the absence of any of the factors known to interfere with the therapeutic effectiveness of liver Various means have been employed to overcome this refractiveness Liver extract or vitamin B_1 intravenously and blood transfusions are helpful for such patients

Macrocytic Anemia of Pregnancy

Although the hematological picture in the macrocytic anemia of pregnancy is similar to that of pernicious anemia, the presence of hydrochloric acid in the gastric secretions of many of these patients serves to differentiate the two diseases Careful studies should be made of each patient to establish the correct diagnosis Most of these patients respond to parenteral liver or vitamin B_{12}, given in the same manner and dose as for pernicious anemia, and a diet providing a high-protein intake well supplemented with vitamins of the B complex Remission with liver or vitamin B_{12} therapy is somewhat slower in these cases than in patients with pernicious anemia

Occasionally the anemia is refractory or responds very poorly to vitamin B_{12} or parenteral liver Better results are obtained in these patients when folic acid 10 to 20 mg, daily by mouth is added for at least 10 days If remission occurs the dose may be reduced to 5 to 10 mg daily When parenteral medication is indicated because of vomiting or diarrhea 15 mg of folic acid daily should be given by the intramuscular route

Patients with severe anemia who show a poor response to vitamin B_1 or liver and folic acid should be given transfusions to carry them through the pregnancy

After delivery the macrocytic anemia usually disappears, and treatment is no longer necessary A diet high in protein and vitamins of the B complex are advised Since this anemia is prone to recur with succeeding pregnancies the diet during subsequent pregnancies must be rich in vitamins of the B complex, and folic acid, 5 to 10 mg should be given daily by mouth as a preventive measure Vitamin B_{12}, 15 to 30 micrograms once a week, should also be given if the preceding measures are ineffective

Other Macrocytic Anemias

Macrocytic anemia may be a complicating factor in pellagra sprue,

Oral therapy with vitamin B_{12} or liver extract is unsatisfactory and is seldom indicated It should not be employed for seriously ill patients those with severe neurological damage or for patients with complicating diseases prone to render liver therapy less effective

Whole liver 200 to 400 gm by mouth daily is effective in inducing a remission and maintaining a normal blood count The liver is to be eaten raw or lightly cooked and may be made more palatable by chopping it in a meat grinder and then thoroughly disintegrating it in a mechanical shaker This pasty material which should contain all fluids as well as the solid liver should then be seasoned with tomato juice or other flavoring to suit the patient and taken in divided doses at mealtimes

Powdered stomach orally 1 oral U S P unit daily is also effective for maintenance therapy The powder may be taken in divided doses, mixed in water milk or fruit juice

Liver stomach concentrates are also effective orally and when given in a dose of oral U S P units daily will induce a remission A maintenence dose of 1 oral U S P unit daily is usually satisfactory

Vitamin B_{12} is also effective in milder cases when given orally The dose is 30 to 50 times that required by the parenteral route

Folic acid although effective in reversing the macrocytic anemia is of no value in relieving or preventing neurological damage It is not recommended in the treatment of pernicious anemia

Since there is variation in the potency of various commercial products *it is essential that the amount to be given be determined by the number* of U S P units Only those preparations approved by the Anti Anemia Preparations Advisory Board of the U S Pharmacopoeia should be employed

Patients with pernicious anemia who are given adequate amounts of vitamin B_{12} or liver invariably respond favorably to therapy Complicating diseases may slow the reaction or necessitate larger doses but the patient sooner or later shows a favorable response Cases not showing prompt improvement must be studied carefully for complicating diseases If none is found the diagnosis of pernicious anemia is erroneous

Patients with pernicious anemia who have exhibited a satisfactory response to therapy and who have subsequently relapsed are extremely rare These patients should be studied carefully since they have usually developed a complicating disease such as carcinoma of the stomach or large intestine

Occasionally a patient develops a temporary refractive period to

and liver are of no value so long as the causative factor is operating, but their use will hasten recovery once it has been eliminated

Restlessness and apprehension, which is causing overactivity should be relieved by morphine sulfate 10 mg, combined with atropine sulfate, 0 5 mg

A whole blood transfusion, always attended with considerable risk in these hemolytic anemias and usually of limited or temporary value is indicated only when symptoms of shock or air hunger are developing If shock is the predominating feature transfusion of plasma alone may prove sufficient When whole blood is given, extreme care must be taken to insure proper matching The blood to be used should be selected from donors with the same blood type as the patient s Cross matching of the patient s cells with the donor's serum and the donor s cells with the patient's serum by the test-tube technique and incubation of the donor s cells and recipient s serum for 1 hour at 37 C are recommended Even with the most careful cross matching, reactions are not uncommon The blood must be given slowly and the patient observed carefully during the infusion Usually 500 cc should be given Repeated transfusions are prone to increase the possibility of reaction

Splenectomy must be considered in patients where no causative factor can be identified and blood transfusions are of no value Cases presenting the pattern of an acute type of hemolytic icterus and those considered to be Lederer s anemia are most likely to benefit from splenectomy Occasionally excellent results are obtained in these patients Usually a good response from splenectomy can be predicted if there is a hyperplastic bone marrow as determined from sternal puncture Corticotropin and cortisone have been shown to be of marked value in helping to control a hemolytic crisis thus enabling surgery to be performed under much more favorable conditions A daily dose of 50 to 100 mg of corticotropin or 100 to 300 mg of cortisone is usually sufficient to give excellent results

Exposure to toxic chemicals should be avoided and infections eliminated

Chronic Hemolytic Anemias

Chronic hemolytic anemias produced by chronic congenital hemolytic anemia with jaundice, erythroblastic anemia and sickle-cell anemia present interesting therapeutic problems

Diphyllobothrium latum infestation severe liver disease and rarely, in functional abnormalities of the gastro intestinal tract such as occur after gastrectomy extensive intestinal resection extensive ulceration and severe diarrhea

Measures should be instituted promptly to correct the basic condition In most cases the anemia clears as the underlying disease is controlled A diet rich in protein containing abundant amounts of vitamin B complex vitamin C and if there is diarrhea vitamin K is indicated

Folic acid given in a dose of 10 to 20 mg daily preferably by mouth is very effective in most of these cases Intramuscular therapy should be reserved for patients who because of vomiting or severe diarrhea may fail to absorb the drug For these patients a daily intramuscular dose of 15 mg is recommended Vitamin B_{12} 15 to 30 micrograms intramuscularly should be given if the anemia is not corrected by folic acid

Other Nutritional Endocrine Deficiency Anemias

Hypochromic microcytic or macrocytic anemias may also occur as a result of deficiencies in vitamin C vitamin K folic acid and in various endocrine disturbances such as myxedema ovarian deficiency and Addison s and Simmonds diseases

Treatment is directed toward amelioration of the underlying disease or deficiency The anemia clears if the initiating cause is corrected

Acute Hemolytic Anemia

This disease caused by infections chemical poisons antigen antibody hemolytic reactions and other miscellaneous causes of unknown etiology presents diverse therapeutic problems If the causative agent is known or can be found and is removed the hemolysis promptly ceases During the acute hemolytic phase these patients must be at absolute bed rest Careful nursing care is essential Chilling is to be avoided Warm blankets electric heating pads and hot drinks by mouth are all helpful Sufficient fluid intake to maintain a daily urinary output of 1500 to 2000 cc is recommended When indicated 5 per cent glucose in physiological saline may be given intravenously to maintain a satisfactory urinary output A diet high in protein and vitamins is desirable Iron

unchecked course for years and present only minor symptoms The more severe cases progress rapidly to a fatal termination Intercurrent infections are serious and in many cases usher in the terminal illness

A well balanced diet high in proteins and vitamins is advised for these patients The fluid intake should insure a urinary output of 1500 to 2000 cc

Where possible, immunization against infections is desirable It is essential to instruct the patient about the importance of careful personal hygiene Minor cuts, furuncles, head colds, sore throats, and other, usually insignificant conditions should receive prompt and careful attention

Patients with gross bone changes or those who have experienced pathological fracture should receive a diet rich in calcium supplemented by dibasic calcium phosphate, 1 0 gm, morning and evening Synthetic oleo-vitamin D (solution of viosterol in oil) orally 10 to 30 drops (0 2 to 0 6 cc) for adults and 15 to 20 drops (0 3 to 0 4 cc) for infants and children should be administered daily in order to insure absorption and proper utilization of calcium

Constipation, when present, should be corrected promptly Milk of magnesia 15 to 30 cc for adults and 4 to 16 cc for children is satisfactory Occasionally diarrhea becomes a problem Aluminum hydroxide gel containing kaolin (Kaomagma), 15 cc, in a small amount of water before meals or after bowel movement is helpful If diarrhea is not checked, 4 cc of the camphorated tincture of opium [paregoric] 3 or 4 times a day for adults is usually effective Children should be given proportionately smaller doses depending on their ages The dose for those from 5 to 12 years should be 1 0 to 2 0 cc 3 or 4 times a day

Splenectomy is without real value in this type of anemia It is followed by a marked and prolonged outpouring of nucleated cells Huge spleens causing severe abdominal distention gastro-intestinal distress or other symptoms however should be removed to relieve the mechanical difficulty

Whole blood transfusions although of temporary value are to be given to replace blood lost during a hemolytic crisis, or when there is an anemia of sufficient degree to produce symptoms No attempt should be made to maintain a normal blood level by transfusions Only enough blood to relieve symptoms and to restore the usual state of the blood is to be given Careful cross matching as described under transfusion for acute hemolytic anemias must be carried out

Chronic Congenital Hemolytic Anemia with Jaundice

Splenectomy is the most valuable therapeutic measure in this disease and should be performed on all cases where there has been a hemolytic crisis or the disease is impairing health Following splenectomy the red cell count rises the jaundice fades reticulocytes decrease and gradually the hemoglobin red-cell count and hematocrit values reach normal Patients lose all symptoms of the disease feel stronger gain back their sense of well being and in children normal growth and development follow Patients exhibiting recurrence of the disease after splenectomy should be explored for accessory spleens Unless accessory spleens are *removed at the time of the original operation they can hypertrophy* and lead to recurrence of the disease Removal of a hypertrophied accessory spleen will produce a prompt return of remission Recurrence however may follow general reticulo endothelial hyperplasia this will not be benefited by search for accessory spleen structures and can be treated only by methods applicable to other forms of anemia

The operative risk in splenectomy is not great In competent hands it is as low as 3 per cent Post operative infection now for the most part can be controlled by antibiotic therapy and is no longer of consequence

In view of the low mortality from splenectomy and the known high incidence of gallstones gallbladder disease underdevelopment in children and the ever present possibility of a hemolytic crisis in unoperated cases splenectomy must be considered seriously in every case even though the disease may be extremely mild Certainly it should be used in any case where there is a possibility of the patient s being so situated that he cannot receive skillful surgery when the necessity arises

Patients in acute *hemolytic crisis should receive the treatment* described for Acute Hemolytic Anemia Splenectomy should be performed as soon as the patient s condition warrants it Occasionally it must be performed under unfavorable conditions during the crisis in order to stop the severe hemolytic process Blood transfusions are much more effective after splenectomy

Erythroblastic Anemia Cooley s Anemia Thalassemia

Treatment for this racial familial anemia is unsatisfactory Milder forms of the disease occurring in adults and children may run a slow

patibility Infusion must be very slow and the patient observed closely for signs of reaction

Cold sponges, baths, douches, and hot enemas are recommended as helpful measures in overcoming circulatory stasis

Patients with severe anemia presenting shock must be kept warm, and the foot of the bed should be elevated Intravenous plasma or whole blood should be given promptly and oxygen administered as long as there is any respiratory distress or evidence of cyanosis

Patients in remission exhibiting chronic stages of the disease are helped by a diet high in protein, vitamins, and minerals Adequate rest and careful personal hygiene are helpful Intercurrent infections, exposure, and overfatigue are to be avoided Chronic infections should be eliminated and patients vaccinated adequately against them Proper dental care and mouth hygiene are important Trauma, especially to the legs, is to be avoided A sedentary occupation is desirable Patients of this type with a hypochromic anemia are benefited by ferrous sulfate, 1 0 to 2 0 gm daily Liver is of no value Steroid hormones may be helpful

Chronic leg ulcers respond slowly and poorly to treatment Prolonged rest, adequate nutrition, transfusions, and vasodilator drugs are advised Relapses usually come less frequently and are less severe as the patient grows older Splenectomy usually is of no benefit but it may be necessary when the spleen is very large

Polycythemia Vera Erythremia

No specific therapy exists but relief for varying periods of time can be secured by measures that bring about a reduction in the blood volume, viscosity, and number of circulating erythrocytes

Patients should be encouraged to avoid a sedentary existence, as circulatory stasis is prone to produce thrombosis A bland diet low in iron — to consist of asparagus, cheese, corn, fish, lettuce, milk, onions, potatoes, rice, squash, turnips and white bread — is advised Foods rich in iron such as beet greens, beans, beef, apricots and peaches, egg yolk, kidney, lamb, liver, molasses, pork, prunes, and raisins should be avoided or taken in limited quantities

Fluids sufficient to insure a daily urinary output of 1500 cc are recommended Dehydration is to be avoided Intercurrent infections should receive prompt and adequate therapy Complicating duodenal ulcer or gout should receive prompt treatment

Cobaltous chloride as a 5 per cent aqueous solution given in a dose of 100 mg after meals 3 times a day may be of some value in the occasional patient

Arsenic copper iron liver, vitamin B complex spleen extract, adrenal cortical extract plasma and various cell extracts raw pancreas hormones, and pentnucleotide are of no therapeutic value in this form of anemia

Roentgen radiation to spleen and long bones is of little or no value but in an occasional case transient relief may be secured

Prevention Since this disease is racial and familial in origin and apparently dependent on the inheritance of a red cell anomaly those who are heterozygous carriers of the disease should not marry other heterozygous carriers and have children

Sickle Cell Anemia

There is no specific therapy available for this and supportive measures are at best unsatisfactory Treatment consists in efforts to prevent acute hemolytic crises management during these crises and supportive measures during remission or in the chronic stage

Hospitalization and complete bed rest are advised for patients exhibiting sudden increase of weakness fatigability episodes of abdominal pain increase in jaundice and a rapidly increasing anemia A diet high in protein carbohydrate and vitamins and sufficient fluid to insure a urinary output of 1 500 cc are recommended Therapy with the proper antibiotic is to be commenced promptly if there is an associated infection

Meperidine (demerol) hydrochloride 100 mg or dilaudid hydrochloride 2 to 4 mg orally or intramuscularly every 4 hours is advised if pain is severe Mild degrees of pain are controlled satisfactorily with codeine phosphate 30 to 60 mg or acetylsalicylic acid 0 3 to 0 6 gm 3 times a day

When symptoms from anemia appear or the hemoglobin falls rapidly transfusions should be given to control the immediate crisis Blood for transfusion must be cross matched carefully at both room temperature and 37 C by the method outlined under transfusion for acute hemolytic anemia Careful Rh studies should be made and compatible blood of the proper Rh group selected to avoid any immediate or future incom

handle these agents A dose of 3 to 6 millicuries intravenously or approximately 25 per cent more of the isotope orally in the form of sodium acid phosphate is recommended Repeated hematocrit, hemoglobin, and erythrocyte checks should be made Usually the single administration results in a satisfactory remission, which persist for from 6 months to 5 years Occasionally it is necessary to repeat the dose to obtain a remission At least 3 to 5 months should elapse before additional isotope is given Repeated administration may be given at 6-month to 1 year intervals should relapse occur

Complications resulting from radioactive phosphorus treatment consist for the most part of thrombocytopenia, leukopenia, or anemia, usually one or the other rarely all three In rare cases, transfusion may be required to control these untoward effects

Radioactive phosphorus, although one of the most satisfactory therapeutic agents available, has some serious drawbacks It is expensive and must be administered by one especially qualified to handle radioactive isotopes finally it may possibly increase the incidence of leukemia in these cases

Nitrogen mustard mechlorethamine (Mustargen) hydrochloride, will also produce remission It is not as satisfactory, however, as radioactive phosphorus A dose of 0 1 mg per kilogram of body weight is recommended No single dose is to exceed 8 mg The calculated dose should be given intravenously daily for 4 days Care must be taken to insure that no extravasation occurs, since injection into the subcutaneous tissue or around the vessel results in severe painful, local inflammation, and thrombosis of the vein may occur The drug is to be dissolved in sterile physiological saline and administered without delay by injecting it into the delivery tubing of an already operating intravenous infusion apparatus, thus avoiding the possibility of extravasation Subsequent administration of the drug should not be given until at least 6 weeks have elapsed Nausea vomiting and anorexia commonly follow injection This can be avoided to some extent if the drug is given in the evening near bedtime and after the patient has been sedated with 0 2 gm of pentobarbital (Nembutal) given intramuscularly and . to 3 gm of chloral hydrate by mouth 1 or 2 hours before injection Diphenhydramine (Benadryl) hydrochloride 50 to 100 mg, or dimenhydrinate (Dramamine) 50 to 100 mg by mouth prior to injection and at 3 hour intervals for 6 to 9 hours subsequently is also helpful in preventing and controlling nausea

Venesection with the removal of 500 cc of blood twice a week until the hematocrit value is reduced to 45 per cent is a fairly satisfactory and simple method of treatment Hemoglobin values although not as satisfactory an index may be used since they parallel the hematocrit If used the hemoglobin should be reduced in males to 12 or 13 gm and in females to 11 to 12 gm Usually 6 to 8 phlebotomies are required in the average case

Venesection is harmless and may be repeated whenever an increase in the hematocrit or hemoglobin indicates the need Care must be taken that repeated loss of iron with the blood removed and low iron intake does not result in a hypochromic polycythemia of severe degree Remissions of from 6 to 18 months are common following this therapy but eventually the polycythemia returns

Patients with high hematocrit and erythrocyte values should receive phlebotomies until these are reduced to approximately 60 per cent and 6 million or better respectively before isotope therapy is given

Roentgen ray therapy administered by a skilled radiologist is useful in some cases especially when with venesection leukocytes increase and *immature forms such as myelocytes appear The best results are secured* by the use of generalized radiation (spray therapy) in which small doses are delivered to multiple sites A dose of 30 roentgens over the entire body from a distance of 2 5 meters at daily intervals until a dose of 300 to 500 roentgens has been given has proved satisfactory The white blood cells of patients receiving radiation therapy must be checked frequently usually biweekly for the first week and daily thereafter If the count falls below 6000 treatment must be stopped Radiation therapy on the whole is not always satisfactory Patients become refractory it is time consuming and in certain cases it may cause toxic symptoms

In recent years treatment with radioactive phosphorus (P_{32}) has proved fairly effective although reports are conflicting The ease of administration the prompt control of the disease claimed in 80 to 90 per cent of the cases and the absence of any immediate untoward effect make it a fairly satisfactory therapeutic agent This radioactive isotope with a half life of 14 3 days can be given intravenously or orally Approximately *75 per cent of the oral dose is absorbed* provided phosphorus precipitants such as calcium aluminum milk and iron are eliminated from the diet for 24 hours before administration and provided no food is given for at least 2 hours after the administration of P_{32}

Administration of the isotope must be made by those qualified to

CHAPTER LII

DISEASES AFFECTING PRIMARILY THE LEUKOCYTES

Diseases affecting the white blood cells may cause a decrease in the number of circulating cells which may be either acute or chronic or cause the formation of abnormal cells, which may increase decrease or have little effect on the total number of white blood cells

Agranulocytosis

The medical emergency resulting from an abnormal destruction or depression in granulocyte production presents a serious therapeutic problem Immediate bed rest, abundant fluids, intelligent nursing care and protection from infection are essential All drugs or medication of any kind are to be stopped immediately Penicillin, 40,000 units intra muscularly every 3 hours, is to be begun and continued until th neutrophils return to the blood in normal values If an infection is present which is apparently penicillin resistant streptomycin aureomycin terramycin, whichever is found to be effective should be given

Patients with severe mouth or throat lesions that interfere with fluid or food intake are to be given intravenous infusions of physiological salt solution containing 10 per cent glucose Nutrition may be maintained further by intravenous infusions of 5 per cent protein hydrolysate and plasma Diluted bland broths by mouth are started as soon as the patient can take them and are to be followed by a bland diet rich in vitamins, especially those of the B complex and vitamin C as soon as the patient can tolerate it Parenteral liver and vitamin therapy are given if oral therapy is impossible for more than one week *Folic acid* 10 to 20 mg daily orally or intramuscularly, and *vitamin* B_{12} 50 micrograms daily, are also recommended although usually they are ineffective

The mucous membranes of the mouth should be rinsed with slightly

SECONDARY POLYCYTHEMIA

Polycythemia secondary to congenital abnormalities of the heart pulmonary arteriovenous aneurysms cardiac decompensation anoxemia and various other causes responds to the measures which correct the causative disorder Patients in whom the causative factor cannot be alleviated are best treated by repeated small phlebotomies if they seem beneficial

capable of producing agranulocytosis Allonal, Alphebin, Amabital Amidoamine, Amidoneonal, Amidophen, Aminopyrine, Amidos, Amidotal Compound, Amifeine, Aminol, Amphenal, Ampydin, Amytal Compound, Antabs, Baramid, Barb-amid Benzedo Compound, Causalin, Cibalgin, Cinchopyrine, Compralm, Cronal, Dymen, Dysco, Eumed Gardan, Gynalgos Hexin, Ipral-Aminopyrin, Kalms, Lumodrin, Midol, Mylin, Neonal Compound, Neurodyne, Nod, Novaldin (Novalgin), Optalidon, Peralga, Phenamidal, Phen-Amidol, Phenopyrine, Pyramidon, Pyraminal, Seeqit, and Yeast-Vite

Unfortunately, these as well as other patented preparations containing aminopyrine can be purchased over the counter in drug stores and other public places It is, therefore, essential that all patent drugs taken by patients be checked Those preparations containing aminopyrine should be discontinued or taken under the careful supervision of a physician Repeated white blood counts and differential blood smears are necessary, if severe disease is to be avoided The white blood count alone gives in sufficient information, since most of the cells in the count may be lymph ocytes and consequently the first signs of neutropenia are missed

Primary Splenic Neutropenia

Treatment in this somewhat rare condition should be splenectomy Supportive measures including bed rest, high-vitamin, high calorie diet, adequate fluid intake and local treatment for infection of the mouth, when present, are all directed toward getting the patient ready for operation Penicillin, 40 000 units intramuscularly every 3 hours, is recommended if there is infection of the mouth or throat, or if the gran ulocytes have fallen below 2,000

Splenectomy will be beneficial in 60 to 80 per cent of patients and is followed immediately by the disappearance of all signs and symptoms, the granulocytes soon return to, and remain at, their normal value

Agnogenic Myeloid Metaplasia

Treatment is unsatisfactory and for the most part directed toward relief of symptoms Splenectomy must not be performed, and radiation therapy is dangerous Exposure to benzol, carbon tetrachloride, or other possible toxic agents or drugs must be avoided A diet high in calories,

Trade names are often confusing and tend in many instances to mask the real composition of the preparation

warm physiological saline 3 or 4 times a day and the mouth must be kept as clean as possible Pain is controlled with acetylsalicylic acid, 0 3 to 0 6 gm or meperidine (Demerol) hydrochloride, 50 to 100 mg, given orally or intramuscularly

Nursing care is directed toward protecting the patient from infection All lesions must be kept clean and protected Decubitus ulcers must be avoided and the rectum and genitals kept scrupulously clean

Blood transfusions are recommended in patients with severe agranulocytosis Repeated daily small transfusions of 250 cc for 3 or 4 days are helpful in serious cases

Pentnucleotide, although usually disappointing may prove helpful in a dose of 10 cc intragluteally approximately . hours after meals, 4 times a day, until there is improvement clinically and the granulocyte count shows a favorable response The dose should then be reduced to 10 cc 2 times a day until the granulocytes are normal If improvement has not taken place after 10 days of pentnucleotide therapy the appearance of a favorable response is unlikely

Dimercaprol injection *U S P* (BAL in oil) is effective in agranulocytosis caused by arsenic mercury, or gold A dose of 3 mg per kilogram body weight should be given every 4 hours for the first and second days followed by 4 injections on the third day and thereafter 2 injections a day for 10 days or until recovery has occurred

Patients with cyclic agranulocytosis may benefit from splenectomy when other therapy has been ineffective

Prevention Since most cases of agranulocytosis develop following the ingestion of drugs all patients receiving medication for any length of time are potential candidates for the disease Especial care including frequent white blood cell counts and differential smear examinations must be taken when patients have been or are being given aminopyrine chloramphenicol chlorpromazine phenylbutazone organic arsenicals sulfonamides thiouracil and x ray therapy

The Pure Food and Drug laws have done much toward protecting the public by requiring that ingredients be stated on the label Fortunately most of the preparations capable of causing agranulocytosis are not common ingredients of patent medicines Aminopyrine is an exception however and is used in numerous preparations The following patented remedies are known to contain aminopyrine unless the drug has been removed since the writing of this book in which case it will be omitted from the label These following remedies are therefore all

capable of producing agranulocytosis Allonal, Alphebin, Amabital, Amidoamine, Amidoneonal, Amidophen, Aminopyrine, Amidos, Amidotal Compound Amifeine, Aminol, Amphenal, Ampydin, Amytal Compound, Antabs, Baramid, Barb-amid Benzedo Compound, Causalin, Cibalgin, Cinchopyrine, Compralm, Cronal, Dymen, Dysco, Eumed Gardan, Gynalgos Hexin, Ipral-Aminopyrin, Kalms, Lumodrin, Midol, Mylin, Neonal-Compound, Neurodyne, Nod, Novaldin (Novalgin), Optalidon, Peralga, Phenamidal, Phen-Amidol, Phenopyrine, Pyramidon, Pyraminal, Seeqit, and Yeast-Vite

Unfortunately, these as well as other patented preparations containing aminopyrine can be purchased over the counter in drug stores and other public places It is therefore, essential that all patent drugs taken by patients be checked Those preparations containing aminopyrine should be discontinued or taken under the careful supervision of a physician Repeated white blood counts and differential blood smears are necessary, if severe disease is to be avoided The white blood count alone gives in sufficient information, since most of the cells in the count may be lymphocytes and consequently the first signs of neutropenia are missed

Primary Splenic Neutropenia

Treatment in this somewhat rare condition should be splenectomy Supportive measures, including bed rest, high-vitamin, high calorie diet, adequate fluid intake, and local treatment for infection of the mouth, when present, are all directed toward getting the patient ready for operation Penicillin 40,000 units intramuscularly every 3 hours, is recommended if there is infection of the mouth or throat, or if the granulocytes have fallen below 2,000

Splenectomy will be beneficial in 60 to 80 per cent of patients and is followed immediately by the disappearance of all signs and symptoms, the granulocytes soon return to, and remain at, their normal value

Agnogenic Myeloid Metaplasia

Treatment is unsatisfactory and for the most part directed toward relief of symptoms Splenectomy must not be performed, and radiation therapy is dangerous Exposure to benzol, carbon tetrachloride, or other possible toxic agents or drugs must be avoided A diet high in calories,

Trade names are often confusing and tend in many instances to mask the real composition of the preparation

minerals, and vitamins is recommended Fatigue, infections, nervous strain, and excessive activity are harmful

If the enlarged spleen hampers movement or if pain is caused by activity, a properly fitted support is helpful Anemia producing symptoms should be relieved by blood transfusions

Leukemia

Therapy in this interesting and fatal disease is for the most part palliative Recent experience with the antifolic acid derivatives has given a dim ray of hope that perhaps more effective therapy may be found

Acute Leukemia

The treatment of acute leukemia irrespective of the cell type is except for the action of antifolic acid compounds of little or no value A supportive regime directed toward conservation of strength, protection from infection and relief of symptoms is recommended Bed rest when there is fever or rapidly progressing disease adequate fluid intake a diet rich in calories minerals and vitamins especially of the B complex and vitamin C pleasant surroundings avoidance of extremes in temperatures and relief from mental tension are essential supportive measures

The mouth and teeth must be kept clean The teeth are to be cleansed after meals with a soft tooth brush and the mouth rinsed with a bland mouth wash such as 1 5 per cent hydrogen peroxide sodium perborate or cetylpyridinium chloride (Cepacol) Patients should be protected from infection Contact with or exposure to individuals with intercurrent infections is to be avoided If infection occurs penicillin should be given When the organism is resistant to penicillin another appropriate antibiotic is to be substituted

Anemia of sufficient degree to produce symptoms of anoxemia should be relieved by blood transfusion Repeated transfusions of 400 to 600 cc of fresh whole blood are recommended This therapy is helpful also when there is bleeding Iron liver, vitamin B_{12} and folic acid are of no value in treatment of the incidental anemia

Arsenic benzol irradiation radioactive phosphorus nitrogen mustards and urethane are of little or no value in acute leukemia Irradiation is contraindicated

Folic acid antagonists warrant therapeutic trial Clinical improvement frequently follows this therapy Acute leukemia may be converted into a subacute or chronic one Aminopterin, 0 5 to 1 0 mg, amethopterin, 3 to 5 mg, amino an-fol, 5 to 50 mg daily by mouth, depending on age, size weight and physical condition, are all useful Aminopterin is the most toxic Therapy must be followed carefully Dosage each day must be guided by physical findings and white-blood cell count Toxic signs calling for cessation of therapy are indicated by a too rapid drop in white cell count, unexplained diarrhea stomatitis, soreness of tongue ulceration of mouth and bleeding Results so far indicate a conversion or slowing in the acute anemia in approximately 50 per cent of these patients No cures have resulted

Cortisone and corticotropin have shown promise in the treatment of acute leukemia in children Cortisone given in a dose of 200 to 300 mg daily produces a temporary palliative effect Children should receive 50 to 75 per cent of the adult dose Corticotropin should be given in a daily dose of 50 to 100 mg

Bleeding at times becomes a most serious problem, and in spite of repeated blood transfusions it continues to exsanguinate the patient Bleeding patients showing an abnormal increase in heparin like substances as shown by the protamine titration test, will receive benefit from protamine sulfate 50 to 100 mg, given intravenously every 4 to 6 hours or toluidine blue 6 to 8 mg per kilogram of body weight daily for 3 to 6 days The latter often proves more effective

Chronic Leukemia

Although treatment probably does not lengthen life much can be done to ameliorate symptoms and give months or years of active comfortable existence Irradiation therapy gives the most satisfactory results in cases with symptoms It affords relief from pressure symptoms produced by enlarged lymph nodes or spleen Weight loss is stopped and anemia fatigue painful or obstructive leukemic infiltrations, purpura and bleeding are all distinctly ameliorated Since radioresistance develops rapidly, patients without symptoms or those presenting minor complaints, which can be controlled by simple measures, should not be given irradiation therapy Irradiation is recommended when there is progressing anemia, fatigue, loss of weight pain and pressure symptoms from infiltrations excessive or uncomfortable lymph node enlargement,

and increasing numbers of immature leucocytes A high white count alone is not sufficient indication for irradiation

Therapy should be directed by an experienced radiologist who decides the technique and dosage to employ Daily white blood cell counts must be taken as a guard against the development of leukopenia and as a guide to the amount of therapy Patients are usually more comfortable if treatment is discontinued before the white blood cells have fallen all the way to normal levels A count of 15 000 to 20 000 is satisfactory provided patients have been relieved of symptoms In the presence of leukopenia or thrombocytopenia irradiation is usually withheld or given with extreme caution In pregnant patients irradiation to the abdomen is to be avoided A relatively high percentage of blast cells suggests a refractory state but is not a contraindication to treatment

Irradiation sickness, manifested by anorexia nausea vomiting, head ache and occasionally diarrhea may present an annoying but usually not a serious problem It is prone to appear with irradiation to the upper abdomen The mechanism of this condition is not understood It may result from injury to the intestinal epithelium or possibly from the release of toxic material from destroyed or injured cells Treatment for the most part is unsatisfactory but certain measures have proved valuable A diet rich in carbohydrates and relatively low in fats taken before irradiation, is helpful The bowels should be evacuated Patients are aided greatly by reassurance and careful explanation about the nature of the treatment Much needless emotional tension fear and later reaction can be avoided by a few kind words of explanation Light cheerful well ventilated rooms are desirable for treatments Individuals prone to develop symptoms may require a smaller dosage and greater intervals between irradiations Several drugs have been used with varying degrees of success Pyridoxine 100 mg given every 4 hours for 2 days before and 3 or 4 days after therapy is helpful Dimenhydrinate (Dramamine), 50 to 100 mg 4 times a day beginning 1 day before and continued for 2 or 3 days after treatment, will prevent nausea in many patients Corticotropin and cortisone also exert a beneficial effect against radiation sickness Chlorpromazine 25 to 50 mg orally or intramuscularly 2 or 3 times a day is the newest and most effective therapy

Irradiation therapy is to be discontinued if it fails to relieve or if it aggravates symptoms when it causes an increase in the anemia, stimulates an increased production of immature cells, or when bleeding occurs, when platelets decrease or fail to increase or when the patient

shows deterioration Roentgen therapy in suitable cases of chronic leukemia may be followed by striking symptomatic improvement Large tumor masses disappear, the enlarged spleen and liver shrink, anemia decreases, platelets return toward normal, the basal metabolic rate falls, and pressure symptoms disappear The patient often gains strength, his appetite improves and he feels his normal self once more

Radioactive agents are also of value in this treatment and may be substituted for, alternated with, or be given concurrently with roentgen irradiation Their effect is similar to that of irradiation, and their use is in general governed by the same principles that control irradiation Radium thorium-x, and radiothorium are of limited value since control of radiation is difficult They have been abandoned for the newer radioactive isotopes

Radioactive phosphorus, produced by the cyclotron or uranium pile and exhibiting a half life of 14 3 days, is an effective agent It is easy to administer gives continuous radiation and, since it is deposited in larger amounts in those areas exhibiting the greatest degree of leukemic infiltration, the radiation is delivered in a most effective manner Radiation sickness is not a problem and seldom develops with therapeutic doses The result of therapy in the chronic myeloid type is nearly as good as that from roentgen irradiation There is a reversal in the abnormal blood findings, and the patient improves in a manner comparable to that observed following roentgen therapy

The isotope is best given intravenously in small divided doses as an isotonic solution of its dibasic sodium salt The initial dose is 1 to 2 millicuries followed by 0 5 to 1 millicurie on the third sixth, tenth, and fourteenth days depending on the degree of bone marrow hyperplasia and on the size and weight of the patient Thereafter, treatment is individualized and governed by the results from the previous therapy The initial level and trend of the leukocyte count and general clinical picture should be the guiding factors If the initial count was high and a favorable trend is observed after the initial therapy, a dose of 0 5 to 1 millicurie given at weekly intervals is effective and safe When the white blood cell count reaches 30 000, therapy is withheld until the status can be evaluated The isotope is then withheld, the dosage reduced or the interval between doses increased Usually a period of 4 to 8 weeks of therapy is given The course is repeated when signs symptoms and blood or bone marrow studies show return of activity

Unfortunately radioactive phosphorus like irradiation depresses nor

mal bone marrow elements and produces leukopenia, thrombopenia and anemia Large doses are capable of causing aplastic anemia These toxic effects unfortunately limit the therapeutic effectiveness of radioactive phosphorus Better results are to be expected in the treatment of chronic myeloid leukemia than in chronic lymphatic or monocytic leukemia

The nitrogen mustards are also useful therapeutic agents They are not as effective in leukemia as in Hodgkin s disease and like roentgen irradiation and radioactive isotopes they are toxic to hemopoietic and other tissue cells The effect is similar to that shown by roentgen irradiation, but results are not as satisfactory

A daily dose of mechlorethamine (Mustargen) hydrochloride 0 1 mg per kilogram of body weight is recommended The total daily dose should not exceed 8 mg A course of 4 to 6 daily injections should be used Usually 4 daily doses prove sufficient The drug is exceedingly irritating to tissue, and venous thrombosis is not uncommon The desired dose is dissolved in 10 cc of physiological saline and injected promptly into the rubber delivery tubing of an already established intravenous physiological saline infusion This procedure reduces the incidence of thrombophlebitis and tissue necrosis and insures that the total dose is delivered

Triethylene melamine a newer compound with a nitrogen mustard-like *activity is also useful It can be given by injection or by mouth* The dose parenterally is 2 to 3 mg for 2 days and subsequent doses of 2 or 3 mg, depending on the patient s status and response to the initial therapy The drug may be given by mouth in a dose of 10 mg for the first week and 5 to 10 mg in subsequent weeks depending on the patient s response More recent experience has lead to a reduction in dose to 3 to 5 mg weekly

Nausea vomiting anorexia and headache commonly occur after injection of these compounds These symptoms usually appear within 3 hours after injection They may be avoided by sedation prior to therapy and the use of Chlorpromazine 25 to 50 mg 3 or 4 times a day

Arsenic *as the solution of potassium arsenite* USP (Fowler s Solution), formerly so widely used, has almost been abandoned following the introduction of roentgen irradiation In recent years interest in it has been revived The universal availability low cost ease of administration, occasional good results in chronic myelogenous and chronic monocytic leukemia and effectiveness sometimes seen after irradiation refractoriness has developed have saved it from discard It is much

inferior to roentgen irradiation, exhibits unpleasant toxic effects, and relapse occurs soon after treatment is discontinued The therapeutic dose is close to the toxic dose, and usually full therapeutic effect is not secured until toxic symptoms of a minor nature appear It is of little or no value in the treatment of chronic lymphatic leukemia

Arsenic must be pushed until the desired therapeutic effect is observed or toxic effects of sufficient severity develop requiring reduction or cessation of therapy Once treatment has begun, it is desirable to have it be continuous Omission of the drug for more than 2 or 3 days is not advisable One of the most effective methods of giving solution of potassium arsenite U S P (Fowler s Solution) is to begin with 0 3 cc mixed with orange juice 3 times a day by mouth immediately after meals, and to increase the dose by 0 05 cc 3 times a day every third day until a dose of 0 6 cc 3 times a day is reached The dose is then increased by only 0 05 cc once each day until a therapeutic effect is observed or toxic reactions become marked If effective, the leucocyte count should approach normal The dose in either case is then reduced by 0 05 cc once a day until the proper maintenance dose is reached, usually this is 0 3 to 0 5 cc 3 times a day This dose is maintained as long as satisfactory results are obtained or until toxic manifestations force a change

If nausea and vomiting prevent effective oral therapy, arsenous acid may be given intravenously An initial dose of 1 0 mg daily increased by 1 0 mg daily until 5 0 mg are being given each day, is recommended The dose is continued for 6 to 10 days and then decreased gradually

When nausea, vomiting and diarrhea develop after only small amounts of the drug and there are no other signs of toxicity, the dose may be given by rectum If indicated twice the dose given orally may be dissolved in a few ounces of water and administered by this route More severe symptoms are usually relieved by stopping therapy for 48 hours and then resuming treatment with slightly smaller doses

Serious complications such as ascites, edema, herpes zoster, peripheral neuritis, stomatitis widespread keratosis of the skin, and generalized weakness may develop from long continued use of potassium arsenite Unfortunately there is no effective therapy for poisoning with arsenite

Urethane is a moderately effective agent in the treatment of leukemia It is not as useful as roentgen irradiation or radioactive isotopes Occasionally it is effective in patients who have become refractory to irradiation The best results in leukemia have been obtained in the treat

ment of the chronic myeloid type and in some cases of monocytic leukemia. A dose of 1 to 5 gm. by mouth daily is recommended. If nausea or vomiting develops, enteric-coated tablets should be tried. Treatment is to be continued as long as there is a favorable effect and no toxic signs appear. Several weeks may be required to secure favorable effects. Continued weight loss out of proportion to the food intake may indicate a toxic effect. Leukopenia, thrombopenia, and anemia can result from overtreatment. Aplastic anemia may develop as a serious complication.

A supportive regime is essential. Rest in bed when there is fever, infection, severe anemia, hemorrhage, or weakness is essential. Fatigue is to be avoided. Patients with high blood uric acid values should receive abundant fluid intake. Sodium salicylate 1.0 gm. 3 times a day, or acetylsalicylic acid 0.3 to 0.6 gm. 3 or 4 times a day, helps to eliminate excess uric acid as does probenecid (Benemid) 0.5 gm. daily, gradually increased to 2.0 gm. as indicated. Probenecid should not be given concurrently with the salicylates. Proper use of these drugs may help to prevent renal damage and the development of attacks of gout in susceptible patients.

Patients with low white blood cell count and those with a high per cent of abnormal white blood cells must be protected from infections. If an infection does develop, proper antibiotic therapy should be given promptly.

A diet high in calories and rich in vitamins is recommended. The mouth and teeth require special attention, and care must be taken to avoid trauma, infection, or bleeding. Bland mouth washes as recommended for acute leukemia are useful, especially when oozing of blood has occurred. Anemia, when severe, is helped by repeated transfusions. Usually, however, transfusions are not often needed, for the anemia responds to measures that relieve the leukemia.

Aleukemic Leukemia

Treatment in leukemia that exhibits an aleukemic phase may be most difficult. Roentgen irradiation administered by a skilled radiologist and followed carefully by frequently repeated laboratory studies of the white blood elements and platelets is indicated if the case is a chronic leukemia and there are pressure symptoms, pain, or severe anemia. Often

excellent results can be secured by careful irradiation therapy Supportive measures, as described for chronic leukemia, are helpful

Chloroma

Treatment is not effective In general, management should follow that outlined for acute leukemia

Splenectomy in Leukemia

In the past few years, more careful studies of the blood and its characteristics under different diseased conditions have shown that various types of hypersplenism may occur with leukemia and leukosarcoma When evidence can be established of hypersplenism, in the form of increased hemolysis of red blood cells (hemolytic anemia), excess destruction of platelets (thrombocytopenia), or sometimes increased destruction of all blood elements (pancytopenia), splenectomy should be considered

In leukemia the presence of an associated hemolytic anemia may be difficult to establish, the fragility test of the red blood cells and the Coombs test alone are not reliable A better index may be a marked increase in fecal urobilinogen

If an associated hypersplenism is suspected, or established, the patient should first be given a course of corticotropin or cortisone, in decreasing daily maintenance doses, and continued for as long as response is satisfactory If the patient does not respond adequately, or improvement fails to continue splenectomy may be tried The spleen may also be removed with benefit when it is very large and causing considerable discomfort As with hypersplenism alone the best results from splenectomy appear to occur in cases in which the bone marrow is hyperplastic, as determined by previous bone marrow study Splenectomy will not cure the leukemia, but under the above circumstances it may temporarily improve the anemia and so prolong the patient's life

CHAPTER LIII

DISEASES AFFECTING MULTIPLE BLOOD ELEMENTS

Diseases or toxic agents that replace, destroy, or injure bone marrow cause changes in several or all constituents of the blood. They all exhibit an anemia. Etiology may be idiopathic, mechanical (myelophthisic), or toxic.

Idiopathic Aplastic Anemia

Treatment is unsatisfactory. Repeated carefully matched blood transfusions are helpful and will prolong life. Activity regulated to avoid fatigue and a diet containing *abundant protein, vitamins and minerals* are recommended. Patients should be instructed about the danger of intercurrent infections and appropriate antibiotic therapy should be given if an infection develops. Exposure to chemicals or the taking of drugs known to affect bone marrow must be avoided. Daily injections of 15 units of concentrated liver extract, 30 micrograms of vitamin B_1, 20 to 80 units of corticotropin, or 100 to 300 mg. of cortisone have all been used without any consistently ameliorative effect.

Myelophthisic Anemia

Treatment is directed toward the underlying disease. If tuberculosis is present, streptomycin and para-aminosalicylic in full dosage may be of some value. Suppression of bone marrow activity by Hodgkin's disease, leukemia, and multiple myeloma are lessened by adequate treatment of these diseases, but in general therapeutic efforts are of little value. Blood transfusions give temporary relief. Splenectomy or irradiation of an

enlarged spleen should not be undertaken, since the spleen may be the seat of extramedullary blood formation Patients should be instructed carefully about the dangers of intercurrent infection, use of drugs, or exposure to agents known to be toxic to bone marrow

Anemia Due to Toxic or Physical Causes

Anemia resulting from injury to the bone marrow produced by a toxic agent or irradiation responds poorly to treatment The cause if known must be removed at once Toxins may be of external or internal origin Those of internal origin are commonly present in chronic renal disease with retention of nitrogenous products severe liver disease, chronic infections and cachexia from neoplasms, and consequently they are not removable Among the known offenders of external origin are arsenic especially organic arsenicals benzol bismuth colloidal silver, dinitrophenol gold salts irradiation mercury rarely, radium, radioactive isotopes some hair dyes, sulfonamides rarely, trinitrotoluene, and volatile insecticides If arsenic is the offender dimercaprol injection U S P (BAL) should be given intramuscularly in a dose of 3 mg per kilogram at 4 hour intervals for the first 2 days, followed by 4 injections on the third day and then 2 injections a day for at least 10 days Treatment should be continued as long as improvement occurs Dimercaprol is also indicated in poisoning with bismuth and gold

Repeated transfusions are helpful some lives may be prolonged for many months, while others may be tided over the acute phase to eventual recovery Ample rest is advisable and when the red blood cell count is below 3 000 000 per cubic millimeter bed rest is recommended The diet should be high in protein vitamins and minerals Intercurrent infections exposure to known toxic agents overactivity fatigue and physical or mental strain must be carefully avoided Iron, liver folic acid and vitamin B_{12} are of no value In an occasional case, cobaltous chloride, given as a 2 5 per cent aqueous solution in a dose of 100 mg after meals 3 times a day is useful

Erythroblastosis Foetalis

Since the discovery of the mechanism of this disease, a much more logical approach to proper management has been possible Pregnant

Rh negative women whose serum on repeated tests during pregnancy is shown to be free of Rh antibodies will experience no difficulty and erythroblastosis will not develop in the infant Women showing mild degrees of sensitization do not usually develop difficulties and may be permitted to go to term The infant in these cases must be observed closely for the appearance of jaundice anemia and other signs of erythroblastosis If any of these develop immediate transfusion of compatible Rh negative antibody free blood is required Usually 10 cc per pound of body weight is sufficient Transfusions should be repeated whenever the red blood cell count falls below 3 million or when signs of deficient oxygen carrying capacity appear Corticotropin in a daily dose of 25 mg given in 4 divided doses at 6 hour intervals is also helpful Potassium chloride by mouth in a daily dose of 0 1 to 0 . gm helps control edema

Patients with moderately high Rh antibody titers and those who have previously given birth to an infant with erythroblastosis will usually have an infant with moderately severe erythroblastosis Pregnancy in these cases should be interrupted approximately 2 weeks before term and the infant should be placed promptly in an incubator and under an oxygen tent Immediate steps should then be taken to perform a moderate exchange blood transfusion Usually 500 cc of compatible Rh-negative antibody free blood is sufficient Following this if developments indicate need small transfusions of 10 cc per pound of body weight are to be given until recovery is permanent Corticotropin is also helpful in these cases

Seriously sensitized women and those who have previously lost infants from erythroblastosis present a serious problem They must be delivered at as early a date as possible to secure a viable infant Prompt exchange transfusion of 1000 cc of compatible blood oxygen tent and incubator existence are essential The exchange transfusions should be carried out by one experienced in the technique When exchange transfusions are impracticable blood transfusions of 10 cc per pound of body weight are to be given and repeated as often as the condition of the infant warrants Corticotropin should be given as recommended for milder degrees of the disease

Infants exhibiting marked edema are benefited by infusions of salt free albumin 10 cc per pound of body weight and potassium chloride by mouth 0 1 to 0 gm if corticotropin is being administered

If the mother has not had an adequate vitamin K intake and the infant

has jaundice, menadione sodium bisulfite, 2 mg daily intravenously or intramuscularly is to be given to the infant until its prothrombin returns to, and remains at normal levels

Prevention Every pregnant woman should be typed for Rh and those found to be Rh negative checked for Rh antibodies The husband of an Rh-negative woman must also be checked for Rh status When an Rh negative woman is found to have an Rh positive husband who is also Rh homozygous the infant will be Rh positive and consequently is likely to sensitize the mother These pregnancies must be followed closely and check of Rh-antibody titer made sufficiently often to ascertain the status of sensitivity

All recipients of blood transfusions and most, especially females in the child-bearing age must be checked for Rh status and only Rh compatible blood given This is essential if sensitivity to the Rh factor in Rh negative patients is to be prevented

It is also essential to check Rh-antibody status in Rh-negative patients, if transfusion reactions are to be avoided in those already made sensitive either from previous transfusions of Rh-positive blood or from repeated Rh-positive pregnancies

CHAPTER LIV

DISEASES CHARACTERIZED BY ABNORMAL BLEEDING

Patients exhibiting abnormal bleeding tendencies usually show abnormalities of various blood constituents or of capillaries Fibrinogen may be congenitally absent or reduced in amount, prothrombin may be low the platelets abnormal or decreased in number and components of blood serum essential to proper hemostasis absent or reduced in amount Diseases in this category include hemophilia and hemophilia like syndromes (hereditary hemorrhagic diathesis) hemorrhagic disease of the newborn, hereditary hemorrhagic telangiectasis and the purpuras

Hemophilia

Management consists in treatment of the acute hemorrhage and its sequelae and in applying all possible measures to prevent future hemorrhages Acute hemorrhage usually responds reasonably well to local therapy and blood transfusions

Local Therapy Local measures consist of careful ligation cautery, pressure and the application of coagulants Whenever possible vessels in any wound should be carefully ligated even though small in caliber Coagulation although convenient and usually temporarily successful frequently leads to further bleeding if sloughing occurs The topical application of thrombin, either dry as a powder or in sterile isotonic salt solution, usually containing 1000 or 5000 N I H units per cc is frequently helpful Packing or covering the bleeding area with absorbable gelatin sponge (Gelfoam) moistened with thrombin (Oxycel) alone is often satisfactory

General Measures Coagulation is improved by blood transfusions, although only temporarily If there has been much blood loss and bleed

ing is brisk 500 to 1000 cc of preferably fresh blood should be given initially Should bleeding continue, small amounts of 100 to 00 cc every 4 to 6 hours depending on need should be given Plasma known to be free of homologous serum hepatitis virus and preferably obtained fresh from one or two donors is also effective and can be given when red blood cells are not needed It is easier to give and there is no necessity to type, or fear of transfusion reactions Usually an initial dose of 500 cc is effective This may be followed by 100 to 200 cc at 4 to 6 hours as needed

Irradiated antihemophilic plasma derived from normal human plasma is useful and may be given intravenously in a dose of 100 to 250 cc as needed to maintain a satisfactory clotting time Usually a single injection maintains clotting time for from several hours to a day or so

Antihemophilic globulin derived from normal plasma is effective and may be given intravenously or intramuscularly The dried powder in a 20 cc vial should be dissolved in 15 to 20 cc of sterile physiological saline and given intravenously Blood clotting time should be reduced within 30 minutes and remain reduced for 12 to 24 hours The dose is adjusted to the needs of the patient and is regulated by following the coagulation time of the blood If given intramuscularly, it is equally effective but more slow acting Usually it is better to avoid intramuscular medication since hematoma formation is common

Unfortunately, repeated transfusions of blood and plasma and injections of antihemophilic globulin often lead to a refractory condition in which none is successful in arresting the hemorrhage When these measures fail there is usually nothing to be gained by the use of such agents as snake venom, ascorbic acid, vitamin P and K, and oxalic acid

Prevention Patients must be instructed thoroughly about the nature of their disease Normal activities should be permitted, but the patient should be cautioned about doing things that might produce trauma, abrasion, or hemorrhage Dental hygiene is important, and teeth must be kept in a good state of repair Extractions should be treated as major affairs, the patient prepared by transfusions, and the tooth socket packed with fibrin foam

Since the disease is hereditary and is passed to sons through affected mothers, female carriers should be warned of the nature of the disease Unaffected males of the family are not carriers of the disease and consequently will not transmit it to their offspring Affected males will pass the trait to their daughters

Hereditary Hemorrhagic Diathesis

These patients closely resemble hemophiliacs in that bleeding occurs readily and may occasionally be fatal Treatment consists of repeated blood or fresh plasma transfusions as described for hemophilia A diet rich in vitamins and minerals is advised Vitamin C intake should be 100 mg daily If there is any decrease in prothrombin vitamin K_1 4 to 10 mg by mouth daily is recommended Vitamin P (Rutin), 20 mg by mouth 3 times a day for 2 or three weeks may be tried if there is increased capillary fragility but results obtained from its use have been disappointing The use of pressure bandages, fibrin foam and thrombin, as recommended for hemophilia are all useful

Patients must be cautioned about surgery, tooth extractions and vigorous activities The bleeding tendency may decrease in adult life

Hemorrhagic Disease of the Newborn

Bleeding in the newborn may be caused by low prothrombin levels resulting from a deficiency of vitamin K For the newborn infant exhibiting bleeding treatment consists of the prompt administration of vitamin K (*Menadione Sodium Bisulfite*), 1 mg intravenously every 6 hours until bleeding ceases If bleeding is severe and dangerous immediate blood transfusion of 5 to 10 cc of matched, citrated blood per pound of body weight is indicated This will stop immediate hemorrhage and give sufficient time for vitamin K action Cases with minor bleeding in non dangerous areas must be observed closely following injections of vitamin K, but transfusion should be withheld since recovery is usually prompt These cases may be given 2 mg of vitamin K intramuscularly, and this dose repeated at 6 hour intervals until the bleeding tendency is con trolled

Prevention Pregnant mothers should receive vitamin K 2 to 4 mg orally for 3 to 4 days prior to delivery, if there is a history of any diarrhea, jaundice, use of mineral oil cathartics or treatment with sulfonamides or antibiotics effective against gastro intestinal organisms In the presence of jaundice the administration of 0 6 gm of bile salts is recommended to facilitate absorption Infants born of mothers with such a history should receive 2 mg of vitamin K intramuscularly immediately on delivery and menandione 1 mg orally for 3 days following delivery

Hereditary Hemorrhagic Telangiectasis

Treatment should consist of careful removal of exposed telangiectases The telangiectatic lesions are to be removed by electrocoagulation Treatment should be carried out only by those skilled in electrocoagulation technique

Vitamin P (Rutin), 30 mg orally 3 times a day is thought by some observers to be helpful if there is bleeding The dose is to be reduced to 20 mg by mouth 3 times a day in the absence of hemorrhage and maintained at this level for 1 month Vitamin P therapy should be resumed at the first sign of hemorrhage Usually, however, no desirable results are secured with this drug

Patients must be cautioned about activities likely to promote bleeding, and frequent careful checks are recommended to ascertain whether there is concealed bleeding, such as may occur in the gastro intestinal tract

Prevention The hereditary nature of the disease should be explained, and patients informed of the danger of the disease in their children

Essential Thrombocytopenic Purpura

Treatment in the acute phase or during an exacerbation should consist of bed rest and limitation of any activities or conditions that increase venous pressure or mechanically obstruct blood flow Expert nursing assistance is most helpful A nourishing diet rich in foods containing iron such as beans, eggs, kidney, liver, lean meats dark meat of poultry, spinach, dried apricots and peaches, figs and prunes, is recommended If there is evidence of vitamin deficiency, it should be supplemented with vitamin C, 100 mg daily, vitamin K, 4 to 10 mg daily Supplemental vitamins in the absence of any deficiency are not helpful

If hypochromic anemia is present, ferrous sulfate, 1 to 2 gm or when indicated the more bland ferrous gluconate, 1 to 2 gm daily in divided doses by mouth after meals is recommended

Patients exhibiting severe blood loss and those bleeding or showing signs of shock require blood transfusion Repeated transfusions may be required in the severely bleeding patient Fresh blood is preferable Occasionally small repeated transfusions of 100 to 300 cc are helpful when bleeding is not severe Corticotropin 40 to 80 units, or cortisone 200 to 300 mg, daily has proved helpful

Complicating diseases such as infections cardiac decompensation and

Hereditary Hemorrhagic Diathesis

These patients closely resemble hemophiliacs in that bleeding occurs readily and may occasionally be fatal Treatment consists of repeated blood or fresh plasma transfusions as described for hemophilia A diet rich in vitamins and minerals is advised Vitamin C intake should be 100 mg daily If there is any decrease in prothrombin vitamin K, 4 to 10 mg by mouth daily is recommended Vitamin P (Rutin), 20 mg by mouth 3 times a day for 2 or three weeks may be tried if there is increased capillary fragility but results obtained from its use have been *disappointing The use of pressure bandages fibrin foam and thrombin* as recommended for hemophilia are all useful

Patients must be cautioned about surgery tooth extractions and vigorous activities The bleeding tendency may decrease in adult life

Hemorrhagic Disease of the Newborn

Bleeding in the newborn may be caused by low prothrombin levels resulting from a deficiency of vitamin K For the newborn infant exhibiting bleeding treatment consists of the prompt administration of vitamin K (Menadione Sodium Bisulfite) 1 mg intravenously every 6 hours until bleeding ceases If bleeding is severe and dangerous immediate blood transfusion of 5 to 10 cc of matched, citrated blood per pound of body weight is indicated This will stop immediate hemorrhage and give sufficient time for vitamin K action Cases with minor bleeding in nondangerous areas must be observed closely following injections of vitamin K *but transfusion should be withheld since recovery is usually prompt* These cases may be given 2 mg of vitamin K intramuscularly, and this dose repeated at 6 hour intervals until the bleeding tendency is controlled

Prevention Pregnant mothers should receive vitamin K 2 to 4 mg orally for 3 to 4 days prior to delivery if there is a history of any diarrhea, jaundice use of mineral oil cathartics or treatment with sulfonamides or antibiotics effective against gastro-intestinal organisms In the presence of jaundice the administration of 0 6 gm of bile salts is recommended to facilitate absorption Infants born of mothers with such a history should receive 2 mg of vitamin K intramuscularly immediately on delivery and menandione 2 mg orally for 3 days following delivery

Non-thrombocytopenic Purpura

Purpura, with a normal number of platelets, or at least a not markedly reduced platelet count, may be caused by a variety of factors such as allergy, infections, toxins, and vitamin lack, or the cause may be unknown The treatment consists of repeated small transfusions of whole blood and the elimination of any causative factors that can be found Corticotropin, 40 to 80 units, or cortisone, 200 to 300 mg, daily, may be tried

Allergic Purpura

This group of non-thrombocytopenic purpuras consists of those commonly associated with allergic manifestations They are Henoch's purpura, Schonlein's purpura, the purpura seen with erythema bullosum, multiforme, nodosum, simplex, and vesiculosum In many cases the presence of allergy is doubtful or at least not demonstrable It also includes the purpura of angioneurotic edema

Treatment during an acute attack consists of measures to remove the toxin and control the symptoms Any drug being taken should be discontinued until it has been proved not to be the causative agent Infections are treated with the proper antibiotic and known allergens or suspicious articles of the diet eliminated The bowels are to be emptied by an enema and an absorbent mixture of kaolin and aluminum hydroxide (Kaomagma), 15 cc given by mouth 4 times a day for 3 days Charcoal, 1 to 2 gm by mouth daily, is often an effective absorbent During the acute phase bed rest is necessary Often none of these measures is effective

Corticotropin and cortisone are helpful in controlling attacks and may give excellent results

Epinephrine (Adrenalin) hydrochloride 0 3 to 0 6 cc of a 1 1000 solution subcutaneously and repeated as needed, is helpful in angioneurotic purpura, as is ephedrine sulfate, .5 to 50 mg by mouth every 3 or 4 hours

Diphenhydramine (Benadryl) hydrochloride, 50 mg by mouth 3 or 4 times a day, or tripelennamine (Pyribenzamine) hydrochloride 50 mg orally 3 or 4 times a day, is helpful and occasionally gives excellent results in allergic purpura If the sedative action of these antihistaminics

ulcers of the digestive tract should receive prompt attention Constipation if present with its attendant straining at stool is to be relieved by an enema and prevented by adding adequate roughage to the diet or administering milk of magnesia 8 to 15 cc or sodium phosphate U S P, 2 to 4 gm at bedtime

Patients in remission or in a chronic phase of the disease should receive essentially the same measures recommended for the acute phase except that bed rest is not necessary and activities need not be so restricted Patients in this phase of the disease can undergo a splenectomy under much more satisfactory circumstances and with a considerably reduced mortality

Splenectomy is a most important therapeutic measure It is indicated when bleeding is not relieved by conservative measures or when there is danger from serious hemorrhage such as may occur in females at menstruation or patients with ulcers of the gastro intestinal tract large hemangiomas or extensive varicose veins When there is interference with normal existence chronic ill health, and impairment of social and economic activities splenectomy is likewise indicated It is of no value in patients exhibiting purpura secondary to infections toxic agents or other diseases Individuals in whom the diagnosis is doubtful should not receive splenectomy

Although splenectomy gives excellent immediate results in nearly 75 per cent of mild cases it does carry a mortality of approximately 3 per cent even in skilled hands and there is always the possibility of recurrence of the thrombocytopenia often however without recurring bleeding This recurrence may be caused by hypertrophy of accessory spleens not removed at the time of operation or the possible development of greater activity by the reticulo endothelial system

Secondary Thrombocytopenic Purpura

Successful treatment depends on discovering and removing the cause of the thrombocytopenia whenever this is possible Blood dycrasias drugs foods infection physical agents plant and animal products are all capable of causing the disease Supportive measures are the same as those described for essential thrombocytopenic purpura Corticotropin or cortisone given in the dosage recommended above may prove most useful

Purpura Caused by Avitaminoses

Lack of vitamin C, vitamin K, and possibly vitamin P may cause purpura Treatment consists in administering the proper vitamin in adequate dosage

Purpura caused by vitamin C deficiency will be relieved promptly by a daily oral dose of 0 3 to 0 6 gm of ascorbic acid

If the purpura is caused by a lack of vitamin K as shown by lowered prothrombin activity, vitamin K, 5 to 60 mg by mouth each day, or, if jaundice is present, a daily intravenous injection of 10 to 20 mg of the vitamin dispersed in glucose will give prompt relief

If there is capillary fragility associated with or causing, the purpura, vitamin P (Rutin), 20 to 30 mg 3 times a day by mouth, may prove helpful

Pruritus can be relieved by diphenhydramine (Benadryl) hydrochloride or tripelennamine (Pyribenzamine) hydrochloride in the doses recommended in the treatment of allergic purpura

Purpura Caused by Toxins

Many drugs commonly employed may cause purpura as a result of idiosyncrasy Bacterial, plant, and animal products as well as chronic heart, kidney, and liver disease may produce purpura occasionally

Treatment should consist of eliminating any drug therapy until it is certain that the disease is not being caused by the drugs being used It may be necessary to employ skin tests and elimination diets to ascertain the causative factor Infections should receive prompt, appropriate therapy Many of these infections such as typhus fever scarlet fever, and cerebrospinal fever respond promptly to treatment Measures recommended for allergic purpura and purpura brought about by vitamin lack are advised if either allergy or avitaminosis appears to be a complicating factor Moccasin snake venom administered in the same manner and dose as recommended for allergic purpura is occasionally helpful and deserves a trial in toxic purpuras Antihistaminic therapy is useful in relieving pruritus Corticotropin and cortisone are frequently very helpful in controlling purpura caused by an idiosyncrasy to an agent, with the withdrawal of the agent the hormone may be discontinued

interferes with their therapeutic use during the day phenindamine (Thephorin), 25 mg may be given orally 3 or 4 times during the daytime and diphenhydramine (Benadryl) hydrochloride, 50 mg, at bedtime

Meperidine (Demerol) hydrochloride 50 to 100 mg intramuscularly is helpful if severe intestinal cramps are present Occasionally morphine sulfate 8 to 15 mg combined with atropine sulfate, 0 5 mg given subcutaneously is required to secure relief Before administration of these analgesics the possibility of an acute surgical condition must be excluded

Amyl nitrite 0 3 cc by inhalation will frequently relieve temporarily a sharp colicky pain of intestinal origin Calcium lactate 1 gm by mouth 3 times a day, or calcium gluconate 10 to 20 cc of a 10 per cent solution intravenously may prove helpful if there is continued severe colicky pain

Moccasin snake venom 0 4 cc subcutaneously . times a week rapidly increased to 1 0 cc 2 times a week, is helpful Treatment is to be continued until hemorrhagic symptoms have been controlled Usually 4 or 5 weeks of this treatment are sufficient A local ecchymosis may appear at the injection site in the first 24 hours and usually a local reaction of sensitivity consisting of a red swollen tender area appears at the injection site about weeks after starting treatment When this appears the dose is to be reduced to 0 05 cc 2 times a week and if the reaction to this dose is not severe it should be continued and gradually increased to 1 0 cc 2 times a week If the reaction to the 0 05 cc dose is severe however the patient must be desensitized by starting with an injection of 0 1 cc of a 1 10 000 dilution and gradually increasing the dose by 0 1 cc amounts up to 1 0 cc of 1 ,000 dilution of venom

Patients exhibiting joint involvement should be in bed and the joint placed at rest Warm applications will relieve pain and swelling Acetyl salicylic acid 1 0 gm 3 or 4 times a day is helpful for joint pain Some caution should be used however as salicylates can cause purpura

After the acute phase subsides measures should be taken to prevent recurrence If the harmful agent is not known skin tests and elimination diets may be tried

It is obvious from the multiplicity of suggested remedies that treatment of this group of purpuras is very far from satisfactory

7 FARBER S Some Observations on the Effect of Folic Acid Antagonists on Acute Leukemia and Other Forms of Incurable Cancer,' *Blood*, 1949, IV p 160

8 KARNOFSKY D A, BURCHENAL, J H ARMISTEAD, G C Jr., SOUTHAM, C M BFRNSTEIN, J L, CRAVER L F and RHOADS C P Triethylene Melamine in the Treatment of Neoplastic Disease, *Arch Int Med*, 1951 LXXXVII, p 477

9 LAWRENCE, J H The Control of Polycythemia by Marrow Inhibition," *Jour Amer Assoc*, 1940 CXLI, p 13

10 LAWRENCE J H LOW-BEER, B V A and CARPENDER, J W J 'Chronic Lymphatic Leukemia A Study of One Hundred Cases Treated with Radioactive Phosphorus," *Jour Amer Med Assoc*, 1949 CXL p 585

11 OSGOOD E E "Titrated Regularly Spaced Radioactive Phosphorus or Spray Roentgen Therapy of Leukemia" *Arch Int Med*, 1951 LXXXVII, p 329

12 PEARSON O H and ELIEL, L P "Use of Pituitary Adrenocorticotrophic Hormone (ACTH) and Cortisone in Lymphomas and Leukemias," *Jour Amer Med Assoc*, 1950 CXLIV, p 1349

13 SILVERBERG, J H and DAMESHEK, W 'Use of Triethylene Melamine in Treatment of Leukemia and Leukosarcoma' *Jour Amer Med Assoc*, 1952, CXLVIII p 1015

14 SPIES T D LOPEZ, G MILANES F TOCA, R and URAMBURN T Oral Versus Parenteral Administration of Vitamin B_{12}" *South Med Jour*, 1949 XLII, p 528

15 STAFF CLINIC 'Hypersplenism *Am J Med*, 1951, XI, p 494

16 STURGIS, C C *Hematology*, C C Thomas, Springfield Ill, 1948

17 WEST, R, and REISNER, E H Jr "Treatment of Pernicious Anemia with Vitamin B_{12}' *Am J Med*, 1949 VI p 643

18 WINTROBE, M M, CARTWRIGHT, G E, PALMER, J G KUHNS W J and SAMUELS L T "Effect of Corticotropin and Cortisone on the Blood in Various Disorders in Man' *Arch Int Med*, 1951 LXXXVIII, p 310

19 LEAVELL B S "Treatment of Sickle Cell Anemia," *Arch Int Med*, 1954 XCIV 801

20 FISHER, J H WELCH, C S, and DAMESHEK W "Splenectomy in Leukemia and Leukosarcoma *N E J Med*, 195-, CCXLVI, 477

Miscellaneous Purpuras

There are often cases of purpura that do not belong to any of the usual categories The more common of these are mechanical and orthostatic purpura resulting from mechanical obstruction of circulation or rupture of capillaries from increased pressure such as occurs in convulsions coughing violent muscular contraction or straining and prolonged standing Purpura simplex fulminans cathectica and David s disease also belong in this group

Treatment of mechanical orthostatic, and cachectic purpuras should consist of measures to prevent abnormal increase in capillary pressure Any deficiency in vitamin C or vitamin P should be corrected as described under purpura caused by avitaminosis Purpura simplex and purpura fulminans should receive treatment as described for allergic *purpuras Corticotropin or cortisone will prove helpful in some of these* patients

Antihistaminic therapy with diphenhydramine (Benadryl) hydrochloride or tripelennamine (Pyribenzamine) hydrochloride will be helpful Either of these drugs will also give relief from pruritus The dose and manner of administration are the same as recommended for allergic purpura

BIBLIOGRAPHY

1 *BERK L BURCHENAL J H and CASTLE W B Erythropoietic* Effect of Cobalt in Patients with or without Anemia *N E J Med* 1949 ccxl p 754

COLLER F A BLAIN A III and ANDREWS G *Indications for and Results of Splenectomy* C C Thomas Springfield Ill 1950

3 CUSTER R P *An Atlas of the Blood and Bone Marrow* W B Saunders Philadelphia 1949

4 DAMESHEK W and ESTREN S Hypersplenism *Med Clin No Amer* Sept 1950 p 1271

5 DAMESHEK W ROSENTHAL M C and SCHWARTZ L I The Treatment of Acquired Hemolytic Anemia with Adrenocorticotrophic Hormone (ACTH) *N E J Med* 1951 ccxliv p 117

6 DIAMOND L K ALLEN F H Jr and THOMAS W O Jr Erythroblastosis Fetalis VII Treatment with Exchange Transfusion *N E J Med* 1951 ccxliv p 39

situ or secondary due to embolism from endocardial valvulitis or mural thrombosis the treatment should consist of measures to relieve the pain When pain is severe, morphine sulfate, 8 to 15 mg, should be used hypodermically at 3- to 4-hour intervals For lesser degrees of pain codeine sulfate, 15 to 30 mg, by hypodermic injection may suffice When perisplenitis and a friction rub are present, a firm, high abdominal binder applied to lessen movement with respiration may decrease the pain caused by respiratory movements

Abscess

Infected emboli may give rise to abscess of the spleen in which case surgical drainage should be carried out, if the abscess is large and involves the entire organ as sometimes happens, the spleen should be removed Adjunctive chemotherapy should be used

Cysts

Small cysts of the spleen are rather frequent and require no treatment Cysts of large size, whether caused by hematomata, dermoids, or parasites such as the echinococcus are treated best by surgical removal when the size of the splenic mass causes very uncomfortable symptoms

Tumors

The chief primary tumor of significance in the spleen is sarcoma The treatment should be surgical removal of the spleen which however, must be done as early in the disease as possible if there is to be a cure The diagnosis may be very difficult, and late removal is not as effective as early excision Diagnostic splenic puncture is best avoided because of the possibility of spread of tumor by this procedure

Amyloid

Amyloid of the spleen may occur as a primary condition or as one secondary to a chronic infection such as tuberculosis, osteomyelitis or other chronic sepsis The treatment should consist of proper therapy

PART XVII

DISEASES OF THE SPLEEN AND LYMPH NODES

CHAPTER LV

DISEASES OF THE SPLEEN

The diseases to be considered in this section are those primarily affecting the spleen and include rupture infarction abscess cysts tumors amyloid primary tuberculosis and congestive splenomegaly (Banti s syndrome) The splenomegaly that occurs as part of a constitutional or blood disorder such as malaria typhoid fever subacute bacterial endocarditis and other infections primary cirrhosis of the liver polycythemia vera leukemia hemolytic anemia purpura Mediterranean anemia Hodgkin s disease lymphoblastomata hypersplenism agnogenic myeloid metaplasia of the spleen and the xanthomatoses is considered under the respective headings of those diseases

Rupture

The manifestations of rupture of the spleen may be immediate or delayed Rupture may follow attempted diagnostic puncture The treatment should consist of removal of the organ for it is not essential to life In rupture of the spleen in malaria during splenectomy care should be exercised by early ligation of the blood vessels at the hilum so that malarial parasites lying dormant in the spleen will not be introduced in the circulation

Infarction

In infarction of the spleen whether primary due to thrombosis in

splenectomy it is advisable if anemia persists The best results seem to occur when splenectomy has been carried out early in the course of the disease rather than late after advanced liver changes have developed Unfortunately however, cirrhosis of the liver may progress in spite of splenectomy When marked hepatic changes have occurred splenectomy is probably contraindicated With manifestations of advanced cirrhosis of the liver with ascites splenectomy should be avoided and treatment should be carried out as outlined under Cirrhosis of the Liver

For severe or recurrent gastric hemorrhage from esophageal varices splenectomy may prove to be curative, however, such hemorrhage may recur at long intervals after the spleen has been removed If the spleen becomes very large and produces discomfort from pressure symptoms it should be removed From these considerations, when an enlarged spleen results from congestive splenomegaly with associated anemia and leukopenia in a young individual with little or no hepatic involvement or with hepatic involvement and resulting gastric hemorrhages or with a heavy bulky spleen, splenectomy should be done The operative mortality unfortunately is high, 20 to 30 per cent

BIBLIOGRAPHY

1 MOSCHOWITZ E The Pathogenesis of Splenomegaly in Hypertension of the Portal Circulation, Congestive Splenomegaly *Medicine*, 1948 xxvii p 187

directed at the underlying infection when one can be found to be present, after eradication of the infection the spleen may undergo regression When amyloid condition of the spleen is cryptogenic no specific treatment is known at the present time General hygienic measures for health should be carried out In either type splenectomy is of no benefit unless the great size of the spleen causes discomfort

Tuberculosis

Tuberculosis primary in the spleen is rather rare The diagnosis may be difficult to establish but when there is a polycythemia tuberculosis of the spleen should be suspected Splenectomy has been successful in some cases of primary tuberculosis of the spleen The results from the use of streptomycin in the treatment of primary splenic tuberculosis have not been satisfactorily determined However streptomycin and para aminosalicylic acid as recommended for pulmonary tuberculosis should be tried

Congestive Splenomegaly Banti s Syndrome

Congestive splenomegaly or Banti s syndrome is a symptom complex consisting of splenomegaly anemia neutropenia and often the late development of cirrhosis of the liver Since Banti s original description there has prevailed considerable controversy of opinion concerning the existence of it as a distinct entity as well as differences of opinion whether splenectomy is or is not the treatment of choice Most are agreed however that a condition occurs in which the spleen is enlarged primarily as the result of increased pressure in the splenic venous system or artery from intrahepatic or extrahepatic causes for which splenectomy may sometimes be helpful The anemia if severe especially after gastric hemorrhage should be treated by repeated transfusions of whole blood If only moderate in degree and of the hypochromic microcytic type which is usual iron should be given either as ferrous sulfate or ferrous gluconate 0 3 to 0 6 gm 3 times a day and this may be helpful Occasionally the anemia may be macrocytic and hyperchromic then anti pernicious anemia therapy with vitamin B_1 or liver extract should be tried in adequate doses Treatment for anemia should be carried out whether splenectomy is performed or not following

health otherwise, and hygienic measures should be directed toward its maintenance

Hodgkin's Granuloma This is the usual form of the disease with multiple foci of enlargement of lymph nodes, splenomegaly, fever, and anemia Sometimes there is invasion of bone and of the nervous system in this form of the disease, although such manifestations are more common in the sarcoma type

At the present time high voltage roentgen irradiation is the preferred method of treatment in localized and early cases of the disease It is best used as a symptomatic measure Ordinarily all areas of lymph node enlargement should be irradiated Irradiation therapy should be given only by a skilled radiologist who keeps in mind the undesirable aftereffects of radiation In beginning the treatment if lymph nodes are large and cause pressure symptoms, or are strategically situated to cause pressure symptoms small doses of irradiation should be given, for the effect of x-ray is often to cause acute edema and swelling of the involved nodes with temporary increase in size, which may be very injurious If there is marked anemia and/or leukopenia, irradiation therapy should be used with caution, on account of its known injurious effect on the hematopoietic system It is best when reasonable to do so to give repeated transfusions to build up the blood before beginning radiation treatment Of the various forms of involvement this type of disease may present the abdominal form is perhaps the most resistant to radiation therapy

Treatment with the nitrogen mustard, mechlorethamine (Mustargen) hydrochloride and triethylene melamine is of definite value The best results are obtained with them in the granulomatous type of the disease as a supplement to deep x ray therapy after irradiation has ceased to be effective or in place of x ray therapy in those cases in which irradiation is ineffective from the beginning Mechlorethamine (Mustargen) hydrochloride is given intravenously in a dose of 0 1 mg per kilogram of body weight dissolved freshly in 10 cc of distilled water and injected into the rubber delivery tube of an already established saline infusion This may be given once a day for 4 days but no single dose should exceed 8 mg Care must be taken to avoid extravasation, for this will cause a severe local reaction Thrombosis of the vein into which the drug is injected may occur occasionally Also care should be taken to give a smaller dose if there is evidence of bone marrow involvement with leukopenia, since mechlorethamine causes a decrease in the circulating

CHAPTER LVI

DISEASES OF LYMPH NODES

Diseases that affect primarily the lymph node structures of the body are Hodgkin's disease lymphosarcoma tuberculosis and sarcoid

Hodgkin's Disease

In a consideration of the treatment of Hodgkin's disease it is well to follow the classification of the disease into three types (1) para granuloma (2) granuloma and (3) sarcoma This is reasonable be cause there are differences in prognosis and therefore corresponding differences in treatment of the different types

Hodgkin's Paragranuloma For this form with its benign course complete lack of invasiveness and usual localization in the neck lymph nodes little or no treatment may be required High voltage roentgen irradiation to the local lymph nodes will cause regression and should be carried out If the nodes become very large and cause symptoms by pressure on adjacent structures surgical excision is indicated Local excision however does not eradicate the disease for often recurrence takes place and in some cases after excision the condition may undergo a change to the more rapidly advancing granulomatous type

Nitrogen mustard therapy in courses repeated as often as necessary as discussed under Hodgkin's granuloma has been used with considerable success in this group However since the prognosis in the uncomplicated case of paragranuloma is relatively good without treatment it makes such therapy difficult to evaluate In cases of paragranuloma treated with nitrogen mustard in which the local lymph node enlargement fails to continue to respond to this form of therapy additional high voltage x ray to the local lymph nodes will usually cause further regression Ordinarily in this type the patient is in good general

(Benadryl) hydrochloride 25 to 50 mg every 4 hours, and aceto phenetidin, 0 3 gm 4 times a day, may be very helpful in relieving pruritus

Hodgkin's Sarcoma This is the most malignant, most invasive type of the disease and also the one most refractory to treatment As in the granulomatous type, at the present time high-voltage x ray therapy is the method of choice, followed by courses of mechlorethamine (Mustargen) hydrochloride as outlined for the granulomatous type, there is some evidence of better results with the combined methods of treatment than with either one alone With bone involvement, marrow invasion and leukopenia irradiation may be given directly to the bone, but the physician must be cautious in the use of either irradiation or mechlorethamine with this manifestation of the disease With central nervous system involvement great care must be exercised in giving irradiation to the skull since this may result in acutely increased intracranial pressure and death

The other measures of treatment should be carried out as outlined for the granulomatous type

Lymphosarcoma

Lymphosarcoma considered by some to be but a different form of lymphatic leukemia but more highly malignant has certain cellular and invasive characteristics that make many continue to consider it is a separate entity It is one of the most malignant forms of lymphoblastomata less responsive to treatment than the usual lymphatic leukemia and for that reason it is included here Both high-voltage roentgen ray and mechlorethamine therapy should be tried as outlined for Hodgkin's granuloma in the preceding pages, but the results are not encouraging Some benefit may be derived from the application of irradiation locally to enlarged lymph nodes that are causing pressure symptoms As in the other lymphoblastomata mechlorethamine (Mustargen) hydrochloride administered after x-ray refractoriness may give additional benefit, although chiefly palliative Life may be prolonged several months thereby, but the outcome is usually fatal

For severe anemia transfusions of whole blood should be given repeated daily or every other day Very great care needs to be used in treating lymphosarcoma with high voltage x ray, for there may occur a sudden severe drop in circulating white blood cells with toxic symptoms of fever, nausea, and vomiting Then almost as suddenly there may be

white blood cells Mild sedatives such as phenobarbital 15 to 30 mg by mouth half an hour before each injection of mechlorethamine and giving the infusion at bedtime may alleviate the nausea and sometimes the vomiting If this treatment does not control the symptoms pentobarbital 0 2 gm parenterally or chloral hydrate 2 gm by rectum an hour before giving the drug is more effective Dimenhydrinate (Dramamine), 50 to 100 mg at 4 hour intervals following the injection, may also help After larger doses of mechlorethamine anemia, thrombocytopenia, and hemorrhagic diathesis occur These should be treated with repeated transfusions and the use of penicillin to prevent infections

An interval of 2 to 3 weeks should elapse between courses of treatment with mechlorethamine to allow hematological recovery from the previous course If blood changes are minimal however and if there is evidence of relapse in the form of fever, lymphadenopathy splenomegaly and so on, a course of treatment may be repeated in 10 days Triethylene melamine is also useful and should be given in a dose of 2 to 3 mg for 2 or 3 days followed by injections once or twice a week as conditions indicate The drug can also be given by mouth in a dose of 10 mg repeated in 5 to 10 mg doses each week as the patient s course indicates Oral therapy is very helpful in far advanced Hodgkin s disease and frequently it gives relief from the fever, itching weakness and anorexia

For the anemia concentrated liver extract, 1 0 cc (15 units) daily intramuscularly vitamin B_{12} and iron as ferrous sulfate or ferrous gluconate, 0 3 gm 3 or 4 times a day by mouth, may be tried but usually these measures are not very helpful Transfusions of whole blood may be required

Between courses of irradiation therapy or between courses of mechlorethamine or triethylene melamine Fowler s solution beginning with 3 minims 3 times a day and increasing 1 minim 3 times a day to a total of 10 minims 3 times a day then decreasing the dosage at the same rate may be helpful

Cortisone and corticotropin have been of no significant benefit in Hodgkin s granuloma

During all the methods of treatment herein outlined when the patient is ill, bed rest is essential preferably in a hospital with full nutritious high vitamin diet adequate fluids and sedatives as may be necessary For the pressure pains that may be present morphine sulfate methadone or methyldihydromorphinone (Metapon) should be used in adequate dosage Pruritus can be a serious problem Diphenhydramine

stitutional symptoms are often lacking and the mortality rate is less than 10 per cent, treatment should be symptomatic The disease occurs largely in Negroes, and in diagnosis great care is required to differentiate it from tuberculosis and syphilis so that measures for those diseases will not be carried out erroneously, these do no good in sarcoidosis It has been estimated that 10 per cent of patients with sarcoidois ultimately develop clinical tuberculosis If that occurs, the treatment for tuberculosis should be instituted

It is thought by some that *uveoparotid fever* is sometimes a manifestation of sarcoidosis The eye lesion under such circumstances may become very troublesome, and either corticotropin or cortisone in dosage of 100 mg a day may be tried with possible benefit The status of steroid therapy is still unsettled in so far as the cutaneous, lymphatic, osseous and visceral forms of the disease are concerned

With pulmonary and mediastinal involvement from this disease, high voltage x ray therapy may be tried, often with benefit Local excision of lymph nodes or roentgen irradiation of superficial ones will do little or no good

BIBLIOGRAPHY

1 JACKSON H Jr and PARKER F Hodgkin's Disease' *N E J Med*, 1944 ccxxx p 1 ccxxxi pp 35 639, ccxxxii p 547 ccxxxiii p 369 ccxxxiv, pp 37 103

LOVELOCK F J and STONE D J Cortisone Therapy of Boeck's Sarcoid *Jour Amer Med Assoc*, 1951 cxlvii p 930

3 ROSS J R and EBAUGH F G Jr Current Trends in the Management of the Leukemias and the Malignant Lymphomas *Med Clin No Amer* Sept 1951 p 1381

4 SILTZBACH L E POSNER, A MEDINE M M "Cortisone Therapy in Sarcoidosis *Jour Amer Med Assoc*, 1951 cxlvii p 9 7

5 SILVERBERG J H and DAMESHEK, W Use of Triethylene Melamine in Treatment of Leukemia and Leukosarcoma' *Jour Amer Med Assoc* 1952 cxlviii p 1015

6 SMALL M J Favorable Response of Sarcoidosis to Cortisone Treatment *Jour Amer Med Assoc*, 1951 cxlvii p 932

7 MIDDLETON W S The Riddle of Sarcoidosis (Hutchinson Boeck Granulomatosis) *Ann Int Med* 1954 xli 465

a sharp rise in the circulation of white cells characteristic of the lympho sarcoma type that is refractory to treatment

Patients with lymphosarcoma are usually quite ill and require rest in bed preferably in a hospital and should be given a nutritious diet adequate in vitamins with all means of supportive and symptomatic therapy to keep them comfortable Such measures are outlined fully in the first chapter

Tuberculosis

Lymph node enlargement from lymphatic drainage of active foci of tuberculous infection in any part of the body is usual On the other hand particularly in children and in Negroes there is often a tuberculous involvement that is primarily in the lymph nodes particularly in the neck the mediastinum and the mesentery with little or no demonstrably active lesion in the lungs or elsewhere This is caused usually by the bovine type of tubercle bacilli The tonsils are considered by some to be the primary focus of cervical lymph node tuberculosis even though they may not appear abnormal

In the treatment of such primary tuberculous lymphadenitis with its low grade chronicity the tendency to spontaneous healing or the tendency to necrosis suppuration and sinus tract formation should be kept in mind

Adequate rest good hygiene and heliotherapy are the general measures that should be instituted and these usually suffice High voltage x ray therapy may be helpful but it has been given up by many because of its tendency to cause undesirable necrosis and tissue breakdown With sinus tract formation surgery followed by heliotherapy is often successful When lymph nodes are large and cause compression symptoms particularly in the neck or abdomen surgical excision may be required Contrary to an older belief adequate surgery with tight closure does not usually result in tissue breakdown and sinus tract formation

Streptomycin para aminosalicylic acid and the isonicotinic hydrazides should be given as recommended for pulmonary tuberculosis They hasten healing and insure resolution of the lesions in a high percentage of patients

Sarcoidosis

In sarcoidosis a chronic benign granulomatous disease in which con

Sinus Pauses

This is a rare type of arrhythmia Its prevention may sometimes be accomplished by removing a focus of irritation, such as an enlarged cervical lymph node or thyroid, by desensitizing an inflamed throat with a spray of cocaine or a lozenge of nupercaine (Nuporals), or by surgical resection of the nerve plexus around an irritated carotid sinus In some cases atropine sulfate in doses of 1 to 2 mg may be effective in the treatment of sinus pauses this failing, ephedrine sulfate may be effective, given by mouth in doses of 25 to 50 mg, or isopropyl arterenol (Isuprel), 2 5 to 5 0 mg under the tongue as needed

Auricular Premature Beats or Extrasystoles

The treatment of these is similar to that for ventricular extrasystoles and is described under that heading

Paroxysmal Auricular Tachycardia

Attacks of paroxysmal auricular tachycardia may often be stopped by any of a variety of vagus stimulations such as holding a deep breath and blowing against the closed epiglottis (Valsalva experiment), the attempt to draw air into the lungs with the epiglottis closed (Muller experiment), bending over lowering the head, drinking very cold water, or swallowing bits of ice inducing gagging, retching, or vomiting by tickling the posterior pharynx, giving syrup of ipecac in 4 to 16 cc doses and by stroking or massaging the carotid sinus or by ocular pressure These vagal stimulating procedures will arrest approximately 20 per cent of the cases

Digitalis preparations are very useful in stopping this arrhythmia Lanatoside C (Cedilanid) in a dose of 0 8 mg given intravenously in a previously undigitalized patient is very effective If reversion does not occur promptly another intravenous dose of 0 8 mg may be given in 15 to 30 minutes Digitoxin or digoxin may also be given intravenously or orally to rapid full digitalization with good effects in these cases Usually digitalis preparations are more satisfactory than quinidine in controlling this arrhythmia

Quinidine sulfate often gives excellent results An oral dose of 0 4 gm

PART XVIII

DISEASES OF THE HEART AND CIRCULATION

CHAPTER LVII

DISTURBANCES OF CARDIAC RHYTHM

To prevent the recurrence of a cardiac arrhythmia which disturbs the patient by its symptoms or which decreases the efficiency of the patient's circulation, is of first importance in treatment. Next in therapeutic importance is to end the arrhythmia as quickly as possible. When it is not possible to stop an arrhythmia, treatment should be directed toward minimizing its disturbing effects. Some arrhythmias have no disturbing effects and need no treatment. In treating arrhythmias it is to be remembered that therapeutic consideration must be given also to the cardiac lesion that may be present as a concommitant or complication of the arrhythmia. This is particularly important if and when this is causative of cardiac decompensation or congestive failure. With very few exceptions treatment of the arrhythmia should be supplementary to the treatment and/or the prevention of the coexisting cardiac decompensation and should not replace treatment that would be given in the absence of the arrhythmia. An arrhythmia infrequently in itself can cause cardiac decompensation; in such a case treatment of the arrhythmia is all that is needed. The arrhythmias that in themselves usually need no treatment are sinus or normal tachycardia and bradycardia, sinus arrhythmia, nodal extrasystoles, delayed A V conduction time, partial and complete block without Adams Stokes symptoms, and bundle branch block.

Prevention should not be attempted when the interval between periods of tachycardia is long, but if attacks recur at fairly short intervals, their prevention is a very important therapeutic problem. Under these conditions prolonged digitalization just short of producing nausea is the treatment of choice. This failing after omission of digitalis, quinidine sulfate should be used in doses beginning with 0.1 gm. 3 times a day, increased progressively to 0.3 gm. 3 times a day if after a reasonable time of use attacks continue to occur. Dosage of quinidine beyond 0.3 gm. 3 times a day is not advisable. Unless reactions to quinidine occur—such as ringing in the ears, nausea, vomiting, diarrhea, feeling of faintness or even syncope—it may be continued for long periods, with cessation from time to time to see if attacks continue to occur. If there are unpleasant reactions from quinidine, quinacrine (Atabrine) may be tried in doses similar to those suggested for quinidine. In some patients these methods fail or such unpleasant reactions as just enumerated develop. Then it is best to give up attempts at prevention and merely treat each attack as it occurs. Often, when it is easy to stop attacks, this procedure is preferable to attempts at prevention.

Auricular Flutter

Digitalis is the most effective drug in the treatment of auricular flutter. The patient should be rapidly digitalized as described under Congestive Failure. Digitalis will slow the cardiac rate. At a certain point auricular fibrillation may appear. When this occurs, digitalis should be stopped and often reversion to normal rhythm will then take place. In some patients normal rhythm will appear following digitalization as a direct reversion from flutter without an intermediate period of auricular fibrillation. In other patients if auricular fibrillation develops it may persist, but fibrillation, as a rule, is more amenable to therapy than is flutter, so that the patient is better off than during continued auricular flutter.

If flutter persists after digitalization, then the digitalis should be continued at a maintenance dose level and quinidine therapy instituted. Give by mouth 3 or 4 daily doses at 4-hour intervals, beginning with a dose of 0.2 gm. and increasing each subsequent dose by 0.1 gm., possibly to a dose of 0.5 gm. or occasionally even higher until auricular flutter ceases and normal rhythm appears. If normal rhythm develops, quinidine should be reduced to a dose of 0.2 gm. 2 or 3 times a day and continued

at 3 hour intervals until the desired therapeutic effect is secured or toxicity appears is recommended Patients who do not respond satisfactorily should be given 0 4 gm at 2 hour intervals on the following day Usually 4 to 6 doses are sufficient and it is rarely necessary to exceed 4 gm If oral medication fails or if the drug cannot be given by mouth, cautious intramuscular injection of quinidine lactate or gluconate as a 15 per cent solution in physiological saline 0 3 to 0 6 gm will occasionally prove successful Intravenous quinidine medication should be avoided except in the rare case If it is used a solution containing 0 6 gm of quinidine lactate in 500 cc of 5 per cent glucose solution is given The drug must be given slowly and the patient observed closely At the first sign of toxicity or control of the arrhythmia the injection should be stopped

Procaine amide (Pronestyl), as described under paroxysmal ventricular tachycardia may be tried but usually it is not too effective in the treatment of auricular tachycardia

Quinacrine (Atabrine) dihydrochloride exerts an effect on the heart similar to that of quinidine and, in an intramuscular dose of 0 3 to 0 6 gm sometimes proves helpful The usual dose of 0 4 gm is dissolved in 10 cc of physiological saline solution containing 1 per cent procaine hydrochloride, divided into two 0 5 cc doses which are injected deep into the gluteal muscles Quinacrine may occasionally terminate a tachycardia that has been resistant to quinidine but in our hands it has not proved to be very effective

Methacholine (Mecholyl) chloride 15 to 30 mgm given subcutaneously or neostigmine (Prostigmine) methylsulfate, 0 5 to 1 0 mg given subcutaneously or intramuscularly, is often effective in a short time but neither should be used for patients with asthmatic or other allergic tendencies and neostigmine should not be used in patients with hypertension If either of these drugs is used a hypodermic of 0 6 to 1 2 mg of atropine sulfate should be at hand and given promptly to counteract any severe reaction

Other drugs employed in reverting supraventricular tachycardia are magnesium sulfate 1 to 3 gm given intravenously as a 20 per cent solution, calcium gluconate 10 cc of a 10 per cent solution intravenously morphine sulfate 10 to 15 mg, phenylephrine (Neosynephrine) hydrochloride 0 3 to 1 0 mg intravenously The latter should not be used if there is hypertension arteriosclerosis or evidence of ventricular irritation

Ventricular Extrasystoles or Premature Beats

In many patients extrasystoles of any origin cause no or only very slight inconvenience or disturbance to the patient and need no treatment beyond possible reassurance If they occur after the use of tobacco coffee, tea, or alcoholic drinks, as sometimes is the case, restriction in the use of these is advisable, especially when the extrasystoles disturb the patient, particularly in causing apprehension If extrasystoles are caused by digitalis, as they often are, the dose of that drug should be reduced

In many patients mild sedation is sufficient to stop or greatly reduce the frequency of these extrasystoles Phenobarbital, 15 mg, or chloral hydrate, 0 3 gm, may be given 2 or 3 times a day, both are usually effective

When extrasystoles of ventricular or other origin are persistingly frequent and annoying, procaine amide (Pronestyl) hydrochloride, potassium chloride, or quinidine sulfate should be given in an effort to stop them or greatly reduce their frequency Procaine amide (Pronestyl) hydrochloride is very useful in suppressing ventricular extrasystoles A dose of 0 5 gm by mouth every 4 to 6 hours is usually sufficient Potassium chloride, 2 0 gm, in fruit juice 3 times a day, is helpful, especially in extrasystoles produced by digitalis when there is low potassium level in the serum Quinidine sulfate is also useful The dose must be determined by trial and error since it is desirable to use as little of the drug as proves effective and usually there is no great hurry A dose of 0 1 gm 2 or 3 times a day should be tried, this may be increased up to 0 4 gm if necessary Often 0 2 gm night and morning will be effective In patients in whom the extrasystoles are disturbing only in the early evening, or are especially so then, a small dose of quinidine, 0 2 gm, given half an hour before the usual appearance of the extrasystoles will often prevent their occurence If the larger doses already mentioned, given 3 times a day, are not effective after a week or 10 days it is wise to discontinue giving quinidine and try procaine amide, since larger doses of quinidine, especially when continued, often give unpleasant reactions

If the extrasystoles are controlled by quinidine, it is wise to decrease the dosage after a week or two and finally omit the drug, to see whether the extrasystoles tend to recur Frequently, after quinidine therapy, extrasystoles may not recur for variable periods

In the case of failure of quinidine or procaine amide therapy, digitalis

at this level, barring unpleasant reactions, until the physician thinks it wise to discontinue it to see whether recurrence will take place If it does, then the preceding procedure should be repeated Quinacrine dihydrochloride (Atabrine) given as described for paroxysmal auricular tachycardia, also may be tried in the refractory case but results are not *very encouraging*

Another recommended way of giving quinidine is 0 4 gm by mouth every 3 hours until the desired or toxic effects appear Usually 4 to 6 doses are sufficient If the case is still refractory, 0 4 gm every 2 hours may be tried if care is taken to avoid serious toxic effects It is of importance when giving quinidine in auricular flutter to take the cardiac rate before each dose the course of therapy should be closely followed by frequent electrocardiographic determinations

Auricular Fibrillation

Digitalis is the drug of choice in the presence of *fibrillation*, *although* only rarely does it stop the fibrillation What it does do is slow ventricular rate and consequently increase circulatory efficiency Digitalis should be given as discussed under Congestive Failure

Patients with acutely developing auricular fibrillation and the rare case of fibrillation without any other evidence of cardiac insufficiency or without any evidence of a myocardial or valvular lesion may be reverted to regular rhythm with quinidine given as already described for auricular flutter Such cases should be studied carefully for possible hyperthyroidism and that condition corrected if it is found to exist At present only rarely should regularization by quinidine be undertaken when *fibrillation has been present continuously for some time* unless there is evidence that it preceded and probably caused cardiac decompensation In other words chronic fibrillation in most patients should be allowed to continue because when regular rhythm is established if that is possible, little improvement in cardiac function may result and reversion to fibrillation soon takes place It is in such patients that attempts to change the fibrillation to regular rhythm by using quinidine often result in marked toxic reactions or even fatality Some physicians are becoming more bold in using quinidine in most cases of auricular fibrillation but in our experience the patient with a very large heart chronic fibrillation and cardiac decompensation does not do well with quinidine and usually reverts back to fibrillation

intramuscularly occurs in approximately 30 minutes and reactions from this type of administration are usually no more serious or frequent than from oral administration Usually it is preferable to the intravenous route when parenteral quinidine must be used Quinidine gluconate can be used in the same dose and manner as quinidine lactate When these preparations are used no antipyrine is given

Instead of intravenous quinidine some prefer to use a 20 per cent solution of magnesium sulfate so that 1 0 gm may be given in a few minutes This injection should be continued until 4 0 gm has been given or until reversion to normal rhythm has taken place Frequent or continuous electrocardiographic recordings should be made so as to recognize at once the reversion of rhythm and stop the introduction of magnesium sulfate before toxic reaction takes place Magnesium sulfate given in this way is also not without risk to the patient

When paroxysms of ventricular tachycardia tend to recur, quinidine sulfate by mouth in doses of 0 2 to 0 3 gm 3 times a day may prevent the recurrence Potassium salts, 1 0 gm by mouth 3 or 4 times daily, may have a similar prophylactic effect Procaine amide (Pronestyl) hydrochloride in a dose of 0 5 gm every 4 hours is also useful in the prevention of recurrence

In paroxysmal ventricular tachycardia digitalis should be avoided as it may accentuate the ventricular rate and be harmful, digitalis is also sometimes a cause of this form of tachycardia

Ventricular Flutter and Fibrillation

If these are recognized they should be treated by intravenous injections of procaine amide (Pronestyl) hydrochloride quinidine or magnesium sulfate as described in the previous section They may occur and recur in brief runs, procaine amide (Pronestyl) hydrochloride, 0 5 gm every 3 hours, or quinidine sulfate in doses of 0 2 to 0 3 gm 3 times a day should be given over a prolonged period of time unless toxic symptoms develop The dose of each drug may need to be increased or decreased to suit the requirements of the individual patient

Complete Heart Block

If syncopal attacks do not occur complete heart block in itself needs

should be given provided the extrasystoles have not been caused by digitalis It is particularly in the presence of some organic cardiac lesion that digitalis is effective in reducing or stopping extrasystoles

In some patients atropine either as atropine sulfate, 0 6 mg 3 times a day or as tincture of belladonna 1 cc 3 to 4 times a day will decrease or end the occurrence of extrasystoles

Paroxysmal Ventricular Tachycardia

Usually this arrhythmia is a serious condition and it may be or may become a desperate situation Procaine amide (Pronestyl) hydrochloride 1 0 gm by mouth, followed by 0 5 to 1 0 gm every 4 to 6 hours should be given at once In unconscious patients and those in serious collapse 0 2 to 1 0 gm dissolved in 5 per cent glucose solution should be given intravenously at a rate not to exceed [illegible]00 mg per minute The blood pressure should be carefully observed and the injection slowed or stopped if the blood pressure begins to drop seriously Continual check with the electrocardiograph is essential to proper control of the intra venous medication Procaine amide (Pronestyl), as a gluconate or hydro chloride may be given intramuscularly in doses of 0 5 to 1 5 gm with effective action in 30 to 60 minutes and with fewer toxic effects than with the intravenous route If procaine amide hydrochloride is ineffective quinidine treatment should be applied promptly, by mouth if possible A test dose of 0 [illegible] gm is given followed in 1 or 2 hours by 0 4 gm at 2 hour intervals until the desired effect occurs or toxicity appears Usually 5 or 6 doses are sufficient and seldom must a total dose of 4 gm be exceeded

When the patient is in a desperate condition quinidine should be given intramuscularly and in the rare case intravenously For this purpose a solution containing 0 6 gm of quinidine lactate given intramuscularly or 0 6 gm dissolved in 50 cc of 5 per cent glucose solution given intravenously at a rate of 1 to 1 5 cc per minute is recommended Constant or frequent electrocardiographic tracings should be made when the drug is given intravenously so as to recognize at once a reversion to normal rhythm When this happens, the injection of the solution of quinidine must be stopped immediately In giving this form of quinidine therapy the physician must recognize that it is a dangerous procedure in the presence of a very serious situation which may end fatally either from the disease or as a result of the quinidine The action of the drug given

important in treatment When the mechanism of such attacks has been found, care should be taken to avoid precipitating it This may be all that is necessary Three types of attacks may occur The commonest type is the sudden slowing in heart rate, or cardiac arrest, for varying periods of time Second in frequency is the attack that produces a fall in blood pressure without bradycardia Finally, there is a rare variety which although not clearly understood, apparently involves the brain There is no change in blood pressure or heart rate in this type

For mild symptoms such as attacks of dizziness with or without a feeling of faintness relief will usually come from taking a deep breath and holding it as long as possible with repetition if necessary When these symptoms follow some known cause such as stooping over, several deep breaths, each held for as long as possible will often prevent their recurrence

In an attack the patient should be kept flat on his back, with head low and clothing loose about the neck A dose of aromatic spirits of ammonia 4 cc diluted with water, or whiskey taken neat should be given If the attack is one of sudden bradycardia, cardiac arrest or hypotension and does not respond immediately 0 3 to 0 6 cc of a 1 1000 solution of epinephrine (Adrenalin) hydrochloride should be given hypodermically, or ephedrine sulfate 25 to 50 mg by mouth Amphetamine (Benzedrine sulfate), 10 to 20 mg by mouth is also helpful as is isopropylarterenol (Isuprel) hydrochloride, 5 to 10 mg sublingually

Atropine sulfate 0 6 mg 3 times a day by mouth, to decrease vagus overaction, may control or prevent attacks, and should be tried If there is no bradycardia or hypotension produced during attacks, and atropine does not give relief, treatment as described for Petit Mal Epilepsy should be tried

In some patients who have oft-repeated severe attacks that are not otherwise controlled and are caused by carotid sinus hyperirritability, surgical treatment is advisable either by stripping the nerves from the carotid sinus or by cutting the nerve to the carotid sinus plexus

BIBLIOGRAPHY

1 BLINDER H BURSTEIN J HOROWITZ E GERSH E and SMELIN R Studies on Effects of Parenteral Quinidine Administration' *Arch Int Med*, 1950 LXXXVI p 917

no special treatment Drugs to increase pulse rate in cases of heart block have not been satisfactory

In complete block if there is cardiac decompensation digitalis should be used as in patients without block, the slow rate is not a contra indication to the use of digitalis although digitalis usually is not as effective as in decompensation without the slowed rate of heart block

If syncopal attacks (Adams Stokes syndrome) appear and electrocardiographic and other studies show that they are due to a too slow rate of the heart rather than to short runs of ventricular tachycardia flutter, or fibrillation a 1 1000 solution of epinephrine (Adrenalin) hydrochloride should be given subcutaneously in doses of 0 3 to 0 5 cc every hour or two If repeated frequent injections are needed, the longer-acting epinephrine in oil as a 1 500 suspension 0 3 to 0 75 cc subcutaneously at 8- to 12 hour intervals is usually more effective In either case, medication should be continued for as long as the tendency to severe syncopal attacks is present For recurring milder attacks, 1 100 epinephrine hydrochloride solution may be inhaled several times a day Instead of epinephrine, ephedrine sulfate in doses of 25 to 50 mg may be taken 3 times a day over long periods of time as a prophylactic against Adams Stokes attacks Atropine sulfate 1 mg 3 times a day by mouth is sometimes effective Isopropylarterenol (Isuprel) hydrochloride in a dose of 5 to 10 mg sublingually has been used by us with excellent results in the treatment of this condition It has the advantage of producing a cardiac accelerating effect without exerting any peripheral vasoconstriction and consequent hypertension Patients can insert the tablets under the tongue as needed to maintain a sufficiently rapid rate to avoid syncopal attacks In an occasional patient digitalis decreases or prevents attacks probably by improving myocardial function this is true especially in patients in whom there is some degree of cardiac decompensation

Carotid Sinus Syncope Vasovagal Attacks

Abnormal irritability of carotid sinus or vagus nerve often causative of dizziness fainting slowing of heart rate, or temporary (or even rarely prolonged) heart standstill should be considered and carefully tested for in any patient complaining of such symptoms Few events can be more frightening to a patient than these consequently when these symptoms occur prompt and effective measures to reassure the patient are most

CHAPTER LVIII

DISEASES OF THE PERICARDIUM

Acute Fibrinous Pericarditis

As this form of pericarditis is often part of an attack of rheumatic fever, vigorous treatment with salicylates is indicated; salicylates in the form of sodium salicylate or acetylsalicylic acid should be given in large doses, [illegible] to 3 gm. 3 times a day after meals, accompanied by half as much sodium bicarbonate; these drugs should be given in solution or in tablets coated to prevent solution in the stomach. If mouth dosage causes nausea, sodium salicylate in solution can be given by rectum following a cleansing enema of tap water in a dose of 6 to 8 gm. once a day. Steroid hormones as described under Rheumatic Fever may be helpful.

If the pericarditis is caused by a pyogenic organism — as may be the case in patients with pneumonia, meningitis, streptococcus septicemia, or other bacterial infection, or in patients with an antecedent or accompanying upper respiratory tract infection, tonsillitis, sinusitis or bronchitis — penicillin, aureomycin, or another antibiotic effective on the particular etiological agent should be given in dosage usual in the treatment of infections with these organisms. If there is reasonable suspicion that the exudate is becoming purulent, an exploratory puncture is indicated, with subsequent treatment as described under Pyopericardium.

All of these patients should be kept in bed and should receive a nutritious diet with sufficient fluid intake to maintain a urine output of 1500 to 2000 cc. daily. Often a light-weight ice bag over the precordium is comforting to the patient; some prefer a hot-water bottle. Pain should be controlled by analgesics.

Pericarditis with Effusion

This should be treated as just described for acute fibrinous pericarditis

2 CLAGGETT, A H Jr Intravenous Use of Quinidine with Particular Reference to Ventricular Tachycardia *Amer Jour Med Sc*, 1950 ccxx p 381
3 DIPALMA J and SCHULTS J E Antifibrillatory Drugs *Medicine*, 1950 xxix, p 1 3
4 GERTLER, M M and YOHALEM S B Effect of Atabrine on Arrhythmias *Am Heart Jour*, 1949 xxxvii p 79
5 GOLD H *Quinidine in Disorders of the Heart* Paul B Hoeber 1950
6 HELLMUTH G A Cardiac Arrhythmias Pathologic Physiology Diagnosis and Treatment *Med Clin No Amer* Jan 1952 p 3
7 KAYDEN H J STEELE, J M MARK L C and BRODIE B B The Use of Procaine Amide in Cardiac Arrhythmias *Circulation*, 1951 iv p 13
8 PORDY, L KOLKER J and LEVY H Paroxysmal Ventricular Tachycardia of Prolonged Duration *Am J Med* 1950 x p 254
9 SOKOLOW M The Present Status of Therapy of the Cardiac Arrhythmias with Quinidine *Am Heart Jour* 1951 xlii p 771
10 YOUMANS W B GOODMAN M J and GOULD J Neosynephrine in Treatment of paroxysmal Supraventricular Tachycardia *Am Heart Jour* 1949 xxxvii p 359
11 BELLET S ZEEMAN S E., and HIRSH S A. Intramuscular Use of Pronestyl (Procaine Amide) *Am J Med* 195 xii p 145

Hemopericardium

If this is caused by rupture of the heart subsequent to cardiac infarction, no treatment will prevail. If it develops from rupture into the pericardial sac of an aneurysm the same is true. If it is of traumatic origin prompt surgical opening of the pericardial sac drainage of it, and suture of the myocardium or ligature of the bleeding coronary vessel may be life saving surgery certainly should be undertaken the sooner the better Sometimes a bloody fluid is found in patients otherwise presenting the clinical picture of pericarditis with effusion these patients should have pericardial paracentesis and other treatment as described for that form of pericarditis

Pneumopericardium

If this brings on tamponade symptoms trochar removal of the air by suction as in pneumothorax should be undertaken If it is complicated by infection and pus formation surgical drainage is necessary If it is of *traumatic origin surgical treatment of the trauma is indicated* If it is due to a gas forming bacterium, drainage with local and systemic use of penicillin or other appropriate antibiotic is indicated Possibly 10 000 to 40 000 units of gas gangrene antitoxin N F should be given but the value of this antitoxin is somewhat questionable

Chronic Adhesive and Constrictive Pericarditis

In the presence of fibrous adhesions in the pericardium there are usually concomitant valve lesions all of rheumatic etiology The pericardial adhesions require no particular treatment, the patient will develop congestive failure which *will* require therapeutic management as described for Chronic Cardiac Valvular Disease

When the cause is other than rheumatic fever especially when it is *staphylococcus or tubercle bacilli, constrictive pericarditis will result* with its characteristic symptoms and signs These patients respond poorly to digitalis and diuretic therapy They often require frequent abdominal *paracentesis* to counteract the pressure of increasing ascites These are the patients who should have cardiodecortication (DeLorme s operation) for the surgical removal of the thickened constricting fibrous tissue about the heart The expected results are so good as to justify the

CHAPTER LVIII

DISEASES OF THE PERICARDIUM

Acute Fibrinous Pericarditis

As this form of pericarditis is often part of an attack of rheumatic fever, vigorous treatment with salicylates is indicated salicylates in the form of sodium salicylate or acetylsalicylic acid should be given in large doses, 2 to 3 gm 3 times a day after meals, accompanied by half as much sodium bicarbonate these drugs should be given in solution or in tablets coated to prevent solution in the stomach If mouth dosage causes nausea, sodium salicylate in solution can be given by rectum, following a cleansing enema of tap water in a dose of 6 to 8 gm once a day Steroid hormones as described under Rheumatic Fever may be helpful

If the pericarditis is caused by a pyogenic organism — as may be the case in patients with pneumonia meningitis, streptococcus septicemia, or other bacterial infection or in patients with an antecedent or accompanying upper respiratory tract infection, tonsillitis, sinusitis or bronchitis — penicillin aureomycin or another antibiotic effective on the particular etiological agent should be given in dosage usual in the treatment of infections with these organisms If there is reasonable suspicion that the exudate is becoming purulent an exploratory puncture is indicated with subsequent treatment as described under Pyopericardium

All of these patients should be kept in bed and should receive a nutritious diet with sufficient fluid intake to maintain a urine output of 1500 to 2000 cc daily Often a light weight ice bag over the precordium is comforting to the patient, some prefer a hot-water bottle Pain should be controlled by analgesics

Pericarditis with Effusion

This should be treated as just described for acute fibrinous pericarditis

CHAPTER LIX

DISEASES OF THE MYOCARDIUM

Circulatory Failure of Acute Infectious Disease

Prompt and effective treatment, including the use of antibiotics, of every patient who has an infectious disease is the best way to prevent circulatory failure

Excessive fluid intake should be avoided in the management of infectious diseases as it may precipitate this type of circulatory failure If it develops measures toward increasing cardiac efficiency do not help much Caffeine, 0 6 to 1 0 gm, or nikethamide (Coramine) 2 to 3 cc of a 25 per cent solution may be tried but their effectiveness is doubtful

Frequent intramuscular doses of 0 3 to 0 6 cc doses of a 1-1000 solution of epinephrine (Adrenalin) hydrochloride 0 1 to 1 0 cc of a 1 per cent solution of phenylephrine (Neosynephrine) hydrochloride or 10 to 20 mg of hydroxyamphetamine (Paradrine) hydrobromide by mouth should be given if blood pressure is low although they may do little good

Digitalis preparations should be used only in those patients with a prior cardiac insufficiency The various camphor drugs and strychnine seem to be ineffective and should not be given Dehydration should be corrected, but fluid by any route should be given slowly never more than enough to correct the existing dehydration With dyspnea or appearance of any cyanosis oxygen should be given by mask or oxygen tent If there is anemia blood transfusion given slowly is indicated, blood plasma also given slowly probably will be helpful These patients should be kept in bed in a comfortable position with all physical exertion reduced to a minimum they should be kept warm and dry particularly if they are sweating as is often the case Restlessness and apprehension should be controlled by sedation as described in Chapter 1 The usual measures to prevent thrombophlebitis and phlebothrombosis should be in

route for drainage of pericardial fluid, but there is the danger of puncturing a large coronary artery with resulting fatal hemopericardium Puncture in the back (5) involves traversing the pleural space and lung, with the danger of causing pneumothorax or producing pleural infection with empyema if the etiology of the hydropericardium is a pyogenic organism this route should be used only when the other routes have failed to tap the pericardium

The etiology of this form of disease of the pericardium is frequently unknown in these cases no specific therapy can be advised In those patients in which the cause is the tubercle bacillus, treatment should be as advised for other forms of tuberculosis, in addition, the pericardium should be drained as often as it refills (which will usually be at relatively short intervals) and washed out with a solution containing streptomycin, part of it to be left in the pericardial sac Doses of 0 3 to 0 5 gm of streptomycin may be instilled each day Rheumatic fever or myxedema may be the cause, if so, these conditions should receive appropriate treatment

Pyopericardium

If there is any evidence of pyogenic infection of the pericardium, penicillin should be given parenterally in the dosage described for Pneumococcus Pneumonia with bed rest, diet, and fluids as outlined for Acute Fibrinous Pericarditis If any signs of accumulating pus appear, in either physical or x ray examination, exploratory puncture of the pericardium should be made If pus is found, it should be removed, the pericardial sac washed out with normal saline solution and penicillin injected into the sac as described for Empyema The causative organism should be identified as soon as possible in the pus and its antibiotic sensitivity determined, if it is sensitive to some antibiotic other than penicillin an appropriate shift should be made If pus continues to form, or if fibrin masses appear on drainage the pericardium should be surgically drained and washed out frequently with normal saline containing the antibiotic to which the infecting organism has been found sensitive Throughout all of this, penicillin or other appropriate antibiotic should be continued either parenterally or by mouth as seems best for its systemic effect, and the patient should receive the general therapy outlined in Chapter 1

treat the rheumatic fever promptly and vigorously as described in the section on that disease but be cautious in the use of digitalis and quinidine as sometimes a fatality may result. Mercurial diuretics, however, seem *safe to use when edema is disturbing* Corticotropin or cortisone may be helpful

Neoplasms

*Treatment of neoplasm of pericardium has been discussed in a pre*vious section The same measures apply for neoplasm of myocardium or heart valve In a rare case surgical removal may be possible but in almost all cases only symptomatic treatment can be given With tumor *metastatic to the heart an arrhythmia* such as supraventricular tachycardia or auricular flutter may occur and often is quite intractable to treatment

Von Gierke s Disease Cardiomegalia Glycogenica

There is no specific therapy for this condition If cardiac decompensation is in evidence the treatment should be that described for Chronic Heart Disease

Amyloid Disease

The general condition amyloidosis should be managed as described elsewhere. *Some improvement in the cardiac insufficiency caused by* amyloidosis of the heart may follow the use of digitalis and other therapeutic measures as described for Chronic Heart Disease

Cardiac Disturbances in Endrocrinopathies

These may occur in hyperthyroidism hypothyroidism (myxedema heart) hyper and hypopituitarism and hyper and hypo adrenalism Of *primary importance* is treatment of the causative endocrinopathy In addition treatment of the cardiac disturbance itself may often be needed as described for Hypotension Shock or Chronic Heart Disease depending on what the manifestations of cardio circulatory disturbance may be

operative mortality to be anticipated — actually a small one in the hands of a skilled surgeon operating before the patient has experienced prolonged cardiac decompensation Often these patients will be restored to an essentially normal condition Any evidences of other tuberculous lesions in these patients should have the appropriate management as described for Tuberculosis

Calcified Pericardium

Calcium deposits in the pericardium, visible in x ray examinations often cause no symptoms, and the patient needs no treatment The deposits may be present in the fibrous tissue of chronic adhesive and constrictive pericarditis, if so, treatment should be as just described for these conditions

Neoplasms

If a benign tumor of the pericardium is causing symptoms, it should be removed by a surgeon If the neoplasm is malignant treatment probably would be ineffective x-ray might be tried

BIBLIOGRAPHY

1 FALK A, and EBERT R V Tuberculous Pericarditis Treated with Streptomycin' *Jour Amer Med Assoc*, 1951 cxlv p 310
2 KERN R A SOLOFF L A SNAPE W J and BELLO, C T Pericardial Effusion Constant Early and Major Factor in Cardiac Syndrome of Hypothyroidism (Myxedema Heart)" *Am Jour Med Sc* 1949 ccxvii p 609
3 WHITE P D Chronic Constrictive Pericarditis, *Circulation,* 1951, iv, p 288

CHAPTER LX

DISEASES OF THE ENDOCARDIUM

Acute Endocarditis

Usually this is a part of or a sequence to rheumatic fever and should be managed by prolonged bed rest with salicylates and other measures as described for Rheumatic Fever If the endocarditis is caused by an organism it should be treated with the antibiotic to which the causative *organism has been found susceptible as described in the next section*

Subacute Bacterial Endocarditis

The causative organism must be identified as soon as possible by blood culture After it has been isolated, its sensitivity to available antibiotics should be determined as a guide to which antibiotic should be used and in what dosage Having selected the antibiotic in this manner, treatment should be started at once Since in most patients *Streptococcus viridans is causative treatment with penicillin is described below*

It is wise to give penicillin from the start in large doses If the infecting streptococcus is found to be abnormally resistant to penicillin the dose should be very large At the present time it seems best in this condition to give penicillin intramuscularly except occasionally in the seriously ill patient when it is advantageous to use the intravenous route For intravenous injections the large vein just below the elbow should be used, from time to time shift from one arm to the other or other veins may be used if the arm vein becomes inflamed or thrombosed The penicillin selected for use should be dissolved in a small amount of fluid so that each cc will contain 5 000 to 10 000 units Whether to use the intra muscular or the intravenous route whether to inject intermittently or continuously seem to be largely matters of individual preference, ap-

stituted, and if these complications occur, anticoagulant therapy should be instituted Physical activity should be limited long after the acute disturbance is over

Acute and Subacute Myocarditis

Complete bed rest is indicated The restless patient should be sedated sufficiently to decrease the restlessness, but deep sedation should be avoided, morphine sulfate, administered hypodermically in doses of 8 to 10 mg repeated as needed to quiet the patient, often gives very satisfactory results What has been said in the previous section about fluid intake, blood and blood-plasma transfusions, oxygen, and so called heart tonics should be applied in treating patients with acute and subacute myocarditis Digitalis should not be given, except possibly if auricular fibrillation appears Any developing arrhythmia should be treated promptly

Return to physical exertion for these patients should be very gradual, this is possibly the most important feature in management

Chronic Myocarditis Chronic Non-valvular Heart Disease

This should be treated as described in the section on Chronic Heart Disease

It is to be emphasized that whether chronic heart disease is caused by a non-valvular (i e myocardial) lesion, a valvular (i e endocardial) lesion, or both, the treatment is similar

Rheumatic Carditis

This is a very important form of heart disease, with involvement chiefly, in so far as cardiac efficiency is concerned, of the myocardium It may occur in the first attack of rheumatic fever or in any of the recurrences of it and cause decompensation It may, and often does occur during the course of chronic rheumatic i e valvular heart disease and may be the precipitating cause of a period or recurring periods of decompensation with congestive failure It is important to recognize rheumatic fever as the cause of the conditions just mentioned so as to

CHAPTER LX

DISEASES OF THE ENDOCARDIUM

ACUTE ENDOCARDITIS

Usually this is a part of or a sequence to rheumatic fever *and should* be managed by prolonged bed rest with salicylates and other measures as described for Rheumatic Fever If the endocarditis is caused by an organism it should be treated with the antibiotic to which the causative organism has been found susceptible as described in the next section

SUBACUTE BACTERIAL ENDOCARDITIS

The causative organism must be identified as soon as possible by blood culture After it has been isolated, its sensitivity to available antibiotics should be determined as a guide to which antibiotic *should* be used and in what dosage Having selected *the antibiotic* in this manner, *treatment* should be started at once Since in most patients *Streptococcus viridans* is causative, treatment with penicillin is described below

It is wise to give penicillin from the start in large doses If the infecting streptococcus is found to be abnormally resistant to penicillin the dose *should be very large* At *the present time* it seems best in *this condition* to give penicillin intramuscularly except occasionally in the seriously ill patient when it is advantageous to use the intravenous route For intra venous injections the large vein just below the elbow should be used, from time to time shift from one arm to the other or other veins may be used if the arm vein becomes inflamed or thrombosed *The* penicillin *selected for use should* be dissolved in a small amount of fluid so that each cc will contain 5 000 to 10 000 units Whether to use the intra muscular or the intravenous route whether to inject intermittently or continuously seem to be largely matters of individual preference, ap-

CARDIAC TRAUMA RUPTURE OF THE HEART

If trauma causes heart rupture, the treatment should be prompt and surgical, as already described under Hemopericardium If trauma causes injury to sternum or fracture or distortion of adjacent ribs, surgical management may be needed to alleviate compression on the heart Even if there is no evidence of injury to any part of the chest wall, there may be contusion or concussion of the heart, which should be treated symptomatically, including the manifestations of shock Any arrhythmia that develops after cardiac trauma should be treated just as it would be under other circumstances Trauma to the heart may cause rupture of a heart valve, if this happens and the insufficiency of the valve causes cardiac insufficiency, the condition should be treated as described for Chronic Heart Disease

BIBLIOGRAPHY

1 ALLEMAN R J and STOLLERMAN, G H 'The Course of Beri beri Heart Disease in American Prisoners of War in Japan," *Ann Int Med*, 1948 xxviii p 949
2 CHRISTIAN H A Clinically the Myocardium,' *Arch Int Med*, 1950 lxxxvi p 491
3 DURANT T M Nutritional Factors in Heart Disease *Ann Int Med*, 1951 xxxv p 397
4 FINE, I, BRAINERD H and SOKOLOW M Myocarditis in Acute Infectious Diseases *Circulation* 1950 ii p 859
5 POMPE, J C. 'Cardiomegalia Glycogenica *Dissert*, Amsterdam, 1936
6 SCHNITKER M A MATTMAN P E and BLISS T L "A Clinical Study of Malnutrition in Japanese Prisoners of War *Ann Int Med*, 1951, xxxv p 69

for tooth extraction, tonsillectomy, or other surgical operation At these times treatment with penicillin should be instituted promptly it should be given in a daily intramuscular dose of 300 000 to 600 000 units of penicillin procaine in aqueous suspension for 48 hours before and for 72 hours after any surgical operation and should be continued until evidences of the infection have disappeared For this purpose penicillin may be given by mouth provided the daily dose is approximately 5 times the intramuscular dose

It is to be remembered that with few exceptions patients with sub acute bacterial endocarditis have an antecedent chronic cardiac lesion usually valvular or congenital which may become worse from the heal ing of the bacterial lesion or at least may not be changed by the treat ment that cures the subacute bacterial endocarditis Consequently all of these patients should be observed and treated as are patients with chronic cardiac lesions acquired or congenital who do not have and never have had, subacute bacterial endocarditis

If the infecting organism is not satisfactorily susceptible to penicillin a different antibiotic such as streptomycin aureomycin terramycin or chloramphenicol should be used in the way just described for penicillin and in the dosage and route found to be most effective for the particular antibiotic to be used Combined penicillin and streptomycin may be very effective against streptococcus viridans

If the offending organism cannot be isolated on repeated blood cul tures, and still the clinical picture is typical of subacute bacterial en docarditis it is advised to treat the patient vigorously with penicillin as outlined above for a period of at least 14 days If the response appears favorable the treatment should be continued for another 7 days There is much to gain today from vigorous treatment as 75 per cent of patients recover from this previously fatal disease Now the cause of death is irreversible cardiac renal or cerebral changes and seldom the infection

Toxic reactions from penicillin in the purified forms are infrequent and are usually not severe enough to compel cessation of it Usually the reactions are allergic in character and of the nature of urticarial or erythematous skin lesions Only rarely will penicillin cause fever It has been observed that patients with skin lesions from penicillin often have the lesions of trichophytosis between the toes When present the trichophytosis should receive appropriate treatment

If toxic reactions persist or are severe a shift to a penicillin O prepara tion or 1 ephenamine penicillin G (Compenamine) should be made In a

parently each gives good therapeutic results The dosage for patients whose infecting streptococcus is quite susceptible to penicillin should begin with 500,000 units each 24 hours If the organism involved is less susceptible to the antibiotic, or if clinical response is not satisfactory, dosage should be increased as indicated so that 750,000, 1,000 000, 2,000 000 or even more units are being given each 24 hours As many as 40,000 000 units have been given daily without toxic effects

Penicillin given as recommended usually brings the temperature to normal in a very few days and blood cultures become negative almost im mediately A positive blood culture after penicillin has been given for 48 hours shows the presence of an organism highly resistant to penicillin In such cases much larger doses of penicillin should be given or another anti biotic to which the infecting organism is more susceptible should be used Additional blood cultures should be made to test the effect of this treatment

Carinamide (Staticin) blocks tubular excretion of penicillin, thereby allowing smaller dosage to maintain a higher concentration of the antibiotic in the blood Its dosage ranges from 1 5 to 4 0 gm every 3 hours, the larger doses being necessary with normal renal excretory function, the smaller in cases with impaired renal function Carinamide is recommended when large doses of penicillin are required to control the in fecting organism

Tubular excretion of penicillin is also slowed by probenecid (Benemid) A dose of 0 5 to 1 0 gm every 6 hours effectively retards the rate of elimination of penicillin and usually increases the plasma concentration of penicillin 2 to 5 times or more This drug is apparently of low toxicity

A general rule that seems safe to follow is to continue penicillin in the most effective dosage for 21 days and then stop If fever returns or blood cultures become positive penicillin should be commenced again, preferably in a dosage larger than that used in the first course of treatment In some patients the fever may represent a period of rheumatic fever and this should be treated with salicylates as described in the sec tion on Rheumatic Fever

All patients who have been apparently cured by the treatment just described should be kept under observation with frequent periods of recording the temperature very 4 hours for 24 hours and with frequent blood cultures All such patients should be warned of the danger from any infection of possible streptococcic etiology or from the necessity

CHAPTER LXI

CARDIAC DISEASE RESULTING FROM CONGENITAL ABNORMALITIES OR FROM OTHER DISEASES

Congenital Heart Disease

Of first importance in the treatment of congenital heart disease is the surgical correction or removal of the lesion when it can be done such as ligation of a persisting patent ductus arteriosus end to-end anastomosis of the aorta after excision of a coarcted portion of the aorta, anastomosis between aortic and pulmonary artery branches and so on This field of activity is rapidly and successfully being extended by surgeons so that an increasing number of patients with congenital heart lesions are being cured or at least vastly improved Surgical treatment of every patient with any suggestion of a congenital heart lesion should be considered jointly by the internist and the surgeon skilled in this type of intra thoracic operation They must use every possible means of accurate diagnosis before deciding on the feasibility or non feasibility of a corrective operation in the patient under study

Any congenital heart disease that is not of the type in which surgery has been successful to date should be treated by the methods described under Chronic Heart Disease These patients will be benefited by such treatment for a varying time depending on the nature of the congenital lesion

Since patients with any form of congenital heart disease have a high incidence of subacute bacterial endocarditis they should be given penicil lin or other antibiotic whenever an infection develops or before and subsequent to necessary removal of teeth or operations on tonsils sinuses et cetera

Prophylaxis The frequent occurrence of congenital heart disease in children whose mothers have had rubella (German measles) during preg

Vol. VIII 353

rare case toxic reactions are so marked and so persisting that it is necessary to use another antibiotic to which the infecting organism is susceptible

At present it is generally believed that the use of an anticoagulant along with an antibiotic does not increase the effectiveness of the latter Anticoagulant therapy may be harmful and is not advised If it is thought desirable to use one, however, Dicumarol, with dosage checked frequently by the level of prothrombin in the patient's blood, should be used as described in the section on Myocardial Infarction

Chronic Endocarditis Chronic Valvular Heart Disease

Treatment is essentially the same (1) whichever valve or valves are deformed, (2) whether the deformity is causative of stenosis or incompetence or insufficiency of the valve orifice, singly or in multiple For treatment see under Chronic Heart Disease

BIBLIOGRAPHY

1 BLOOMFIELD A L 'The Present Status of Treatment of Subacute Bacterial Endocarditis,' *Circulation*, 1950 II p 801
2 BURWELL J M, and KIRBY W M M 'Effectiveness of New Compound Benemid in Elevating Serum Penicillin Concentration' *J Clin Invest*, 1951 XXX, p 697
3 EDITORIAL 'Treatment of Subacute Bacterial Endocarditis' *Jour Amer Med Assoc*, 1951, CXLV, p 734
4 ERNSTENE A C 'The Prophylaxis of Subacute Bacterial Endocarditis' *Cleveland Clin Quart*, 1951, XVIII p 1
5 FRIEDBERG C K Subacute Bacterial Endocarditis Revision of Diagnostic Criteria and Therapy, *Jour Amer Med Assoc*, 1951 CXLIV p 527
6 HUNTER T H 'Bacterial Endocarditis A Review,' *Amer Heart Jour*, 1951 XLII p 472
7 LITTMAN D and SCHAAF R S 'Therapeutic Experiences with Subacute Bacterial Endocarditis with Special Reference to Failures' *N E J Med* 1950 CCXLIII p 248
8 RAPPAPORT, B and ELLIS L B The Effect of Subacute Bacterial Endocarditis on the Course of the Underlying Heart Disease, *N E J Med*, 1948, CCXXXIX, p 951

patient, his understanding of it, even if it cannot be removed (which obviously is desirable) will accomplish as much in the treatment of a cardiac neurosis as it will in other types of neurosis Often the precipitating cause of a cardiac neurosis is found to be some chance remark of a physician the patient has not understood or has misinterpreted The physician should always keep this possibility in mind in talking with or writing to his patient Reports to patients of the results of periodic examinations are often the precipitating factor in a cardiac neurosis It is also highly inadvisable for a physician to dictate notes on a patient in the presence or hearing of the patient

Vitamin B_1 (Thiamine) Deficiency Beri beri Heart

The most important therapy for these patients is the giving of adequate amounts of *thiamine hydrochloride 20 to 50 mg daily by mouth*, unless there is marked cardiac decompensation When the latter is present, 50 mg daily intravenous doses are preferable If symptoms of cardiac insufficiency are marked or persist digitalis and other therapy as described for the treatment of Chronic Heart Disease should be begun and continued until all evidences of cardiac insufficiency disappear Not infrequently there is a combination of Vitamin B_1 deficiency and chronic valvular and/or chronic myocardial disease *the latter in addition to the myocardial condition caused by Vitamin B_1 deficiency*

It is being realized more and more that in addition to what has been strictly called beri beri caused by thiamine deficiency general undernutrition is frequently a factor in chronic heart disease a factor that should not be overlooked in the treatment of the patient Such features as nutritional anemia hypoprothrombinemia and other vitamin deficiency states must be recognized *with full utilization of all the dietetic and supplementary measures available to modern medicine for their correction in addition* to the treatment of the cardiac failure

Acute Cor Pulmonale

Arising most often from acute obstruction of the great arteries of the lung usually from a large thrombus escaping from the venous system and lodging in the pulmonary artery or some of its major branches this should be treated as described for Pulmonary Embolism The

nancy, especially when it has occurred in the early weeks of pregnancy, suggests strongly that this infectious disease, and possibly others, may be causative of congenital heart disease Thus, it is important to protect mothers as far as possible against having an infectious disease during pregnancy and to treat such disease, if it does occur then, promptly and effectively, as a prophylactic procedure that may prevent the development of at least some congenital heart lesions

Cardiac Neurosis Effort Syndrome Irritable Heart Neurocirculatory Asthenia

Cardiac neurosis occurs both with and without organic heart disease, with and without arrhythmia. When there is no evidence of organic heart disease, it is important to convince the patient of this fact immediately The physician must take a detailed history and make a very careful physical examination with laboratory study of blood, urine, and stools, electrocardiograms, an x-ray examination including fluoroscopy of heart and lungs with careful measurement of heart size, and a basal metabolism if indicated — all completed before telling the patient in simple understandable words that he has no organic heart disease but that his symptoms are of a nervous nature, that they will not progress into a true heart disease, and that they are curable, although it may take time to bring about such a cure Then treatment should be that appropriate to any other neurosis, as described on page 872 It is possible that a careful history will reveal a precipitating cause, if so, this cause is to be removed as part of the plan of treatment. Obviously to accomplish this will require both time and repeated interviews, for, as a rule, much important information will not be obtained at the first session with the patient

If the patient reveals an arrhythmia, it must be diagnosed accurately by electrocardiogram and then treated as described under the various sub headings of the chapter on Disturbances of Cardiac Rhythm

If a patient with evidence of organic heart disease also has symptoms indicative of cardiac neurosis (and such are present in a large majority of patients with organic heart disease), the management of the neurosis must be added to those measures appropriate to the type of organic heart disease that is present

Prophylaxis If a precipitating cause can be found by questioning the

CHAPTER LXII

CHRONIC HEART DISEASE

Treatment of chronic heart disease is considered under six headings (1) general methods of management, (2) treatment in the stage of very slight or no cardiac insufficiency (3) treatment in the stage of developed cardiac decompensation or congestive failure (4) treatment after cardiac decompensation or congestive failure has had effective management (5) modifications of treatment for certain special forms of chronic heart disease, (6) management when cardiac therapy begins to fail

General Methods of Management

Certain features of the treatment of chronic heart disease are of a general nature and are applicable in some degree at all stages of the disease They may be summed up as measures to decrease the load on the circulation by reducing the work required of the heart These will enable a heart of decreased efficiency to function so as to produce no symptoms To attain this these measures will need to be applied with increasing strictness as time goes on Eventually they will no longer prevent symptoms but for a long time they can minimize their severity Also there is much evidence that the application of these general measures will slow the progession of cardiac insufficiency Some of these general measures should be put into effect as soon as a diagnosis of chronic heart disease has been made preferably before symptoms appear

A *planned life* for the patient with chronic heart disease is very important The physician must study the activities of his patient in great detail and particularly he must find out how the patient and his circulation are affected by what he does in his daily life This cannot be done in a brief interview but requires repeated interviews of consider-

possibility of surgical removal of the thrombus should be considered.

Prophylaxis is very important and should consist of the use of anticoagulants or of vein ligation (as described in the section on Phlebothrombosis and Thrombophlebitis) in all patients in whom vein thrombosis is probable or has already commenced. These methods will prevent pulmonary thrombosis and acute cor pulmonale in many patients.

Chronic Cor Pulmonale

Since this condition is caused primarily by fibrosing lesions of the lung parenchyma and its arteries, treatment should be directed so far as possible toward these lung lesions, together with therapy for the resulting cardiac insufficiency. Recent development of thoracic surgery in the treatment of many forms of chronic pulmonary disease has opened up new ways of treatment of chronic cor pulmonale. Patients with chronic cor pulmonale causing cardiac insufficiency should receive digitalis and other forms of treatment as described in the chapter on Chronic Heart Disease, except that morphine should be used with great caution in the presence of chronic cor pulmonale. The measures recommended for relief of chronic bronchitis and pulmonary fibrosis frequently relieve chronic cor pulmonale.

Prevention. Early recognition and treatment of pulmonary lesions likely to progress and cause cor pulmonale are very important. The patient should be warned against inhaling dust, particularly dust particles that may cause various pneumonoconioses, including silicosis, anthracosilicosis, chalicosis, asbestosis, possibly anthracosis, and others.

accomplished by an intelligent cardiac patient wisely guided by his physician

Considerable activity in the milder sports can be permitted for the patient wise enough to realize that any exercise that causes considerable breathlessness or marked fatigue should be curtailed or stopped completely Beginning a sport for the first time is not recommended and should be undertaken if at all only after very serious consideration on the part of both patient and physician *Walking however is never a* new sport or activity in this sense and the physician may well prescribe continuance of the walking to which his patient is habituated or often advise more of it

In many respects mental activities and sedentary occupations like physical work and sport, need to be decreased intelligently when there is resultant continuing fatigue and difficulty in relaxing and in sleeping

A part of the patient s planned life is concerned with *hours in bed* and *other periods of rest and relaxation* Nine hours in bed each night should be obligatory even in the early stages of chronic heart disease ten hours would be better Many patients will need to train themselves to sleep long hours by practicing muscle and mental relaxation but this can and should be done A glass of milk or a warm bath at bedtime is often conducive to relaxation and sleep but too much preparation and thought may lead to wakefulness A rest period of some kind after luncheon is desirable For many men an after luncheon cigar or pipe is conducive to rest and relaxation Cigarettes are not so restful Women too need to be taught how to relax for many of them this is difficult to learn, sewing and knitting scarcely are in the category of relaxation

Whether to use *sedatives* in the early stages of this disease should receive serious consideration from the physician The easy way to control nervous tension and poor sleeping is to use sedatives but this practice seems undesirable for the cardiac patient except in the stage of decompensation A long continued course of the disease and its disabilities should be expected and for this reason sedatives are of questionable value It is better to train the patient gradually to relax by simple methods and particularly to use the psychological approach generally applied in the management of psychoneuroses refrain from giving any sedative drug or only one if necessary for any unusual restlessness in the early stages of treatment In the experience of the authors chronic cardiac disease before the stage of circulatory decompensation can be managed satisfactorily without giving a sedative drug and after it has developed by using very little sedation

able duration, the physician must gain the patient's confidence and understanding It is good if the physician can arrange to visit his patient's home soon after the diagnosis of heart disease has been made, for there he will see what the patient has attempted to describe in answer to questions about his daily activity

In short, the physician can plan the life of the patient with chronic heart disease so as to adjust it as well as possible to the limitations potential and actual set by the condition of his circulation, only if he knows in great detail how his patient lives, how he works and plays, what his business and family problems are, what his worries are and how he reacts to them what his business is and what physical and mental strains it places on him, with all this and more the physician must familiarize himself, if he is to plan ideally the life activities of his patient and, more important to secure his patient's thorough co operation in carrying out the plans

The physician must maintain an attitude of optimism, making the patient believe that with appropriate restrictions a life of comfort and satisfying activity will be possible for a long time—for many patients for a very long time It is to be remembered that many patients having chronic cardiac disease die with rather than from, heart disease Although, as a rule chronic heart disease will be progressive in its disabling of the patient and will finally be fatal, yet in few disorders is there so much that the physician can do to lighten discomfort and slow progression of the disease Optimism about results of treatment is fully justified

An important feature of a planned life for the cardiac patient is the degree of permissible *physical and mental activity* Shortness of breath is a valuable index of whether activity is too great Equally revealing is fatigue particularly when it persists after a reasonable rest period A persisting rapidity of pulse is another useful index With these as guides the physician can plan intelligently the activity appropriate to each patient

In general strenuous physical activity should be decreased early This may be an important consideration in deciding about the patient's occupation Only rarely however is it necessary to change this abruptly if the patient has consulted the physician early in the development of his cardiac condition It is better to bring about gradual decrease in physical activity by modifying the kind of work a patient does instead of stopping it entirely and having him undertake some new business or other activity Often it is surprising how much physical work can be

cate the need for the more active treatment described in the next section This plan is based on the belief that heart hypertrophy is a harmful rather than a beneficial process, and that giving digitalis will retard the development of hypertrophy of the heart Both animal experiment and clinical observation in man support this view For this purpose digitalis should be given as described on page 712

Treatment in the Stage of Developed Cardiac Decompensation or Congestive Failure

As soon as any of the symptoms of this stage in the progression of chronic heart disease develop it is time to begin a more active plan of management part of which is negative and part of which is positive

Rest Rest soon becomes a necessity for the patient with cardiac decompensation or congestive failure For most patients this means rest in bed, for some patients short or long periods propped up in a chair

The *bed* for the heart patient should be comfortable for the patient and easy to manage The usual hospital bed which is relatively narrow and rather high so that the nurse can easily minister to the patient with a minimum of stooping is ideal Such a bed should have a mechanical arrangement allowing it to be raised easily at the head end and flexed at the level of the patient s knees to permit him to change his position with a minimum of exertion for both him and the nurse This bed should have wheels with those at the foot end swiveled so that the bed can be easily moved by one person A narrow table long enough to *stretch across the bed and having legs with casters should be provided* on this the patient s tray toilet articles, books et cetera can be placed and the patient can lean forward and rest his arms on it The bed should have some form of woven springs and a mattress chosen for comfort A disadvantage of this bed is that there is usually too little to protect the patient from getting cold but this can be remedied by placing one or several thick blankets between mattress and sheet It is well to pur chase such a bed for the patient s home use they are available in any well equipped hospital

How strict should bed regime be? For most decompensated patients twenty four hours in bed is recommended but not for all The patient who has difficulty in urination and defecation when using a urinal or bedpan and many do should be allowed to use a bedside commode the male may stand to urinate and often this is very important for older men These procedures may be distinctly less of a strain on the heart

able duration, the physician must gain the patient's confidence and understanding It is good if the physician can arrange to visit his patient's home soon after the diagnosis of heart disease has been made, for there he will see what the patient has attempted to describe in answer to questions about his daily activity

In short the physician can plan the life of the patient with chronic heart disease so as to adjust it as well as possible to the limitations, potential and actual set by the condition of his circulation, only if he knows in great detail how his patient lives, how he works and plays, what his business and family problems are, what his worries are and how he reacts to them what his business is and what physical and mental strains it places on him, with all this and more the physician must familiarize himself if he is to plan ideally the life activities of his patient and, more important to secure his patient's thorough co operation in carrying out the plans

The physician must maintain an attitude of optimism, making the patient believe that with appropriate restrictions a life of comfort and satisfying activity will be possible for a long time—for many patients for a very long time It is to be remembered that many patients having chronic cardiac disease die with, rather than from, heart disease Although as a rule chronic heart disease will be progressive in its disabling of the patient and will finally be fatal yet in few disorders is there so much that the physician can do to lighten discomfort and slow progression of the disease Optimism about results of treatment is fully justified

An important feature of a planned life for the cardiac patient is the degree of permissible *physical and mental activity* Shortness of breath is a valuable index of whether activity is too great Equally revealing is fatigue particularly when it persists after a reasonable rest period A persisting rapidity of pulse is another useful index With these as guides the physician can plan intelligently the activity appropriate to each patient

In general strenuous physical activity should be decreased early This may be an important consideration in deciding about the patient's occupation Only rarely however is it necessary to change this abruptly, if the patient has consulted the physician early in the development of his cardiac condition It is better to bring about gradual decrease in physical activity by modifying the kind of work a patient does instead of stopping it entirely and having him undertake some new business or other activity Often it is surprising how much physical work can be

cate the need for the more active treatment described in the next section This plan is based on the belief that heart hypertrophy is a harmful rather than a beneficial process, and that giving digitalis will retard the development of hypertrophy of the heart Both animal experiment and clinical observation in man support this view For this purpose digitalis should be given as described on page 712

Treatment in the Stage of Developed Cardiac Decompensation or Congestive Failure

As soon as any of the symptoms of this stage in the progression of chronic heart disease develop it is time to begin a more active plan of management, part of which is negative and part of which is positive

Rest Rest soon becomes a necessity for the patient with cardiac decompensation or congestive failure For most patients this means rest in bed for some patients short or long periods propped up in a chair

The *bed* for the heart patient should be comfortable for the patient and easy to manage The usual hospital bed which is relatively narrow and rather high so that the nurse can easily minister to the patient with a minimum of stooping is ideal Such a bed should have a mechanical arrangement allowing it to be raised easily at the head end and flexed at the level of the patient s knees to permit him to change his position with a minimum of exertion for both him and the nurse This bed should have wheels with those at the foot end swiveled so that the bed can be easily moved by one person A narrow table long enough to stretch across the bed and having legs with casters should be provided on this the patient s tray toilet articles, books et cetera can be placed and the patient can lean forward and rest his arms on it The bed should have some form of woven springs and a mattress chosen for comfort A disadvantage of this bed is that there is usually too little to protect the patient from getting cold but this can be remedied by placing one or several thick blankets between mattress and sheet It is well to purchase such a bed for the patient s home use they are available in any well equipped hospital

How strict should bed regime be? For most decompensated patients twenty four hours in bed is recommended but not for all The patient who has difficulty in urination and defecation when using a urinal or bedpan and many do should be allowed to use a bedside commode the male may stand to urinate and often this is very important for older men These procedures may be distinctly less of a strain on the heart

Weight reduction for overweight cardiac patients without edema is a very important part of reducing the load on their circulation and should be begun very soon after the diagnosis has been made Weight should be reduced by proper dietary restrictions as described in the section on obesity Weight should be lost slowly, a loss of 1 to 2 pounds per week will suffice for the majority of patients If overweight is marked however, weight reduction can be speeded up, but only when the patient is under hospital observation If weight reduction has not been commenced before symptoms of decompensation appear, it should be carried out with the patient hospitalized and at the same time undergoing treatment for the decompensation

It is important that the cardiac patient gain no weight unless he is very thin from some nutritional malady, weekly weighing should be insisted on If any gain in weight is noted, the physician should at once determine whether or not it has been caused by a developing edema If so more active therapy as described previously, should be instituted, if not greater reduction in food intake should be directed It is always important to distinguish, so far as possible between weight caused by edema and natural body weight which is largely adipose tissue

A reduction in diet has an additional advantage for the patient with chronic heart disease a lessened calorie intake decreases the patient's metabolism and is in itself a rest measure

Another important part of the treatment of chronic heart disease is the *maintenance of the patient's morale* He is facing an unknown and to him a serious even dangerous situation In the mind of the laity heart disease is a major calamity The physician must allay the patient's fears and guide him to a rational actually optimistic view of his future while impressing on him the great importance of following meticulously what the physician advises

Treatment in the Stage of No or Slight Cardiac Insufficiency

It is in this early stage of heart disease that the measures just described should be begun with modifications according to the patient's temperament and the physician's belief about the present and potential seriousness of the condition of the circulation and the probability of its rate of progression This is probably the only treatment needed at this stage

If at this stage the heart shows considerable enlargement some believe that *digitalis* should be given in moderate dosage, i e dosage small enough not to cause any toxicity, to be continued until symptoms indi

recommended The patient *should be encouraged to make frequent* changes of position in bed and to move his legs about The nurse can help by *periodically turning* the patient from side to side *Long periods* on the bedpan are conducive to stagnation in the leg veins and must be avoided Short periods out of bed, *if cardiac insufficiency is not too* great, are often advisable The patient's legs should be inspected often *and carefully to detect signs of venous thrombosis* If it is present many now advise heparin or Dicumarol to prolong the clotting time of the blood Others advise prompt ligation of the saphenous vein at groin level to keep emboli from going to the lungs Even if an infarct has already developed in the lungs one or the other of these procedures should be carried out With such prophylaxis embolism will be a less frequent and less serious complication of cardiac disease

Diet For the first few days of treatment (never more than 7 and rarely that long) of a patient with cardiac edema the *Karell diet* of 800 cc of milk divided into 4 feedings is admirable Since this is a starvation diet with very low fluid content some prefer to add lactose and varying amounts of water After the Karell diet any easily digestible food divided into 4 feedings may be given many prefer to make up the needed calories with an excess of carbohydrates while others prefer more protein and fat with less carbohydrate A *low calorie value* 800 to 1000 is desirable so long as cardiac insufficiency is sufficient to make continuance of bed life seem necessary When the patient begins out-of bed physical activity, calorie increase is advised but remember that the cardiac patient should not put on weight and that the *diet should* be rich in vitamins and not made up to any great extent of bulky items of low calorie value

Sodium should be restricted especially when edema is present The following low sodium diet is satisfactory

Low Sodium Diet

Food Allowed

1 Meat boiled fish *or* poultry prepared and served without salt
2 Egg—1 daily
3 Milk—limited to 2 glasses (1 pint)
4 Vegetables—(as desired) any fresh or frozen vegetables except lima beans prepared and served without salt
5 Fruits—(as desired) fresh canned stewed
6 Breads—only yeast bread prepared without salt

than the in-bed struggle to urinate and/or defecate Occasionally, compulsory bed treatment increases dyspnea and may even precipitate pulmonary edema Such patients do better if they are allowed to sit in a comfortable chair rather than forced to remain in bed, because the amount of blood to enter the right auricle from the legs is thus lessened as is the bood that may accumulate in the lungs when left ventricular failure has not improved proportionately, with the result that the right heart delivers blood faster than the left can take care of it Some advise placing wooden blocks 8 to 9 inches high under the legs of the bed at the head end The observant physician and the intelligent patient can work out the desirable exceptions to the general rule of 24 hours in bed for decompensated cardiac patients

A nurse is an important adjunct in the care of patients at this stage of chronic heart disease She should be skilled in nursing technique and she should be selected to suit the temperament of the patient She should be of genial temperament, naturally optimistic, and not very talkative She should entertain but never tire her patient Her necessary ministrations to the patient should not be crowded together without rest periods to prevent fatigue of the patient She and the physician should keep visitors from tiring the patient Visitors should be selected by the physician Their number each day and the length of their visits should be determined by the physician with the nurse ending the visit tactfully but promptly as soon as the predetermined time is up

Patients with chronic heart disease in the stage of marked insufficiency have a considerable incidence of *embolism* either from mural thrombi in the heart or from thrombi in the peripheral veins, especially those in the legs The emboli from the heart may go either to the lungs or to the viscera supplied by the peripheral arterial system, while those from the peripheral veins go to the lungs Emboli will produce symptoms and signs dependent on what organs they lodge in and the size of the emboli Pulmonary embolism, with either sudden death or infarction of the lungs, is the most frequent type of embolism Little can be done to prevent embolism from mural thrombi in the heart but much can be accomplished in prophylaxis against thrombosis of leg veins and consequent embolism to the lungs It seems to the authors that heavy sedation so commonly practiced at the present time in the management of cardiac patients is an important causative factor in the formation of thrombi in leg veins because it makes for increased stagnation of blood by reducing to a minimum the change of body position and movement of the legs. Consequently, heavy sedation for the cardiac patient is not

11 Avoid dried fruits such as figs dates raisins apricots and prunes
12 Avoid lima beans fresh or dried
13 Sodium containing medicines such as soda bicarbonate sodium bromide soda mints Tums Alka-Seltzer and various in digestion powders should not be used Salt gargles and tooth pastes containing sodium are also forbidden

Recipe for Salt Free Bread

6½ lbs bread flour
10 oz sugar
8 oz shortening (Primox)
4 oz. yeast
2 qt water

This makes six loaves Apparently this bread takes a little longer to rise than ordinary bread

Sodium free salt substitutes help make the diet more palatable to most patients There are several of these substitutes available of which Neocurtasal Co salt and Diasol are examples Diasol contains no am monium chloride and so an expectorant action is avoided If a salt substitute is used as salt is used the result will be bitter For most successful use, the salt substitute should be used very sparingly

Understandably many individuals find a low sodium diet monotonous even unpalatable and will not adhere to it Consequently some clinicians prefer to give a mercurial diuretic frequently and allow the patient a more palatable diet containing more sodium Many patients do well with a diet not so restricted in sodium and some do badly on a restricted diet because they need salt The physician should watch for symptoms of salt deprivation and when they appear add sodium chloride to the diet at once or give it separately

Still another approach to a low sodium regime in patients who dis like a low sodium diet such as that outlined above or who have anorexia for solid foods is the application of a 50 mg sodium diet This consists of a mixture of sodium chloride free milk powder (Lonalac) 250 gm sugar, 125 0 gm in water 2000 cc made fresh daily flavored with a pinch of vanilla and served cold This is to be supplemented with 500 cc of orange juice containing 30 0 gm of sugar The orange juice is to be alternated every 2 to 3 hours with 200 to 300 c feedings of the mixture above

7 Cereals—any cooked cereal prepared without salt The only dry prepared cereals allowed are puffed rice, puffed wheat, shredded wheat, and muffets
8 Potatoes and rice, prepared without salt Macaroni spaghetti, and noodles contain salt and are not to be used
9 Butter—unsalted or washed butter
10 Desserts—custards junkets and plain puddings made with salt free milk (Lonalac) and with no added salt, jello, pies with no salt added to the crust and the filling prepared with fresh or canned fruit (no meringues)
11 Beverages—tea coffee carbonated drinks, or fruit juices
12 Flavorings — cocoa chocolate, caramel, maple, peppermint, lemon orange, vanilla maraschino cherries, cloves, cinnamon, allspice nutmeg, ginger, and coffee
13 Seasonings—pepper (black or red) curry, dry mustard, mint, dill vinegar parsley, paprika, sage, thyme, onion garlic, pimento rosemary
14 Sweets—white or brown sugar, honey, molasses, jellies jams, marmalade, or preserves that do not contain sodium benzoate

Special Instructions

1 No salt is to be used in preparation of food or in cooking or to be added to the food after it comes to the table
2 Avoid all canned foods that have salt added, such as canned meats and fish vegetables soups, tomato juice, and V 8 cocktail
3 Avoid all brine cured and smoked foods, such as bacon, ham, pickles smoked fish meat or sausage, and olives
4 Omit all salty foods such as salted nuts, potato chips, and buttered or salted popcorn
5 The following food accessories are also to be omitted because of their salt content meat extracts and sauces, chili sauce catsup mustard and relishes
6 Do not give any cheese clams, oysters, lobsters
7 Use only yeast breads prepared without salt
8 Use no foods prepared with baking soda or baking powder, such as soda crackers biscuits muffins, cakes and cookies
9 Use only unsalted or washed butter Sweet butter may have salt added so be sure to read the label before using it
10 Homemade mayonnaise may be used if prepared without salt

TABLE XV

DIGITALIS PREPARATIONS CARDIAC GLYCOSIDES

Preparation	*Digitalis Purpurea*		*Digitalis Lanata*		*Strophanthus Gratus*	*Strophanthus Kombe*
	Digitalis	*Digitoxin*	*Lanatoside*	*Digoxin*	*Ouabain (Strophanthin G)*	*Strophanthin K*
U.S.P.	Digitalis Capsules Injection Tablets Tincture	Digitoxin Injection Tablets	Lanatoside C Injection Tablets	Digoxin Injection Tablets	Ouabain Injection	
N.F.						Strophanthin K Ampules
Proprietary	Digalen Injectable solutions Tablets	Cardigin Tablets	Cedilanid Ampuls Tablets			
	Digicardium Capsules Tablets	Crystodigin Ampuls Tablets	Digilanid Ampuls Liquid Suppositories Tablets			
	Digifolin Ampuls Liquid Tablets	Digisidin Ampuls Tablets				
	Digiforts Ampuls Kapseals Tablets Tincture	Digitaline Nativelle Ampuls Solution Tablets				
	Digiglusin Ampuls Liquid Tablets	Purodigin Ampuls Tablets				
	Digital Liquid					
	Digitora Tablets					

Fluid intake totaling not more than 1800 to 2000 cc' should be the rule This may be increased in hot weather, or if the patient sweats for any reason The former practice of great restriction in fluid intake caused unnecessary discomfort, often these patients were actually dehydrated Even with marked edema dehydration was present, as shown by dry parched lips, tongue, and throat, and a dry skin Uncomfortable thirst should not be allowed If the sodium in the diet is kept very low the patient can take as much fluid as is needed to satisfy his thirst without increasing his edema This is true also with a more liberal diet and with frequent doses of a mercurial diuretic If the patient is mentally sluggish or weak as often is the case, fluid should be given by the nurse at regular periods in a measured amount

Care of Bowels Vigorous catharsis formerly utilized particularly as a means of removing excess body fluid, is no longer advised The patient with cardiac insufficiency needs a mild cathartic or an enema in just the same way as do other patients i e to prevent disturbing constipation When the diet is low in residue as it often is for these patients a daily bowel movement by mild cathartic or enema is not needed The abdominal distention in cardiac patients, is rarely caused by constipation

Digitalis is needed by almost every patient who has evidences of cardiac insufficiency The kind of digitalis preparation used is relatively unimportant, the amount given is very important and should be determined by the physician in relation to the day-to-day condition of the patient s circulation There are many digitalis preparations available, some suited only for oral dosage, some suited only for intravenous use some suitable for either route, intramuscular and rectal dosage with digitalis preparations is sometimes desirable In addition to the U S P digitalis preparations there are many proprietary preparations When produced by reputable pharmaceutical companies these are effective forms of digitalis and are to be used in the same way as the U S P preparations The physician will do well to confine himself to the use of very few digitalis preparations and thus be thoroughly familiar with their therapeutic effectiveness Since various powdered leaf preparations differ in strength it is wise to select one variety and use it continually

The word digitalis is used here to mean any preparation having an effective digitalis action not preparations of digitalis purpurea alone The most important digitalis preparations in frequent use at present, together with the average daily dosage for each, are listed on the following pages

The patient with well marked congestive failure who is not already receiving digitalis or has received none for 10 days should be digitalized with pills, tablets or capsules of powdered digitalis The following plan is advised 0 3 gm (5 cat units) 5 times the average daily dose, should be given, followed by 0 5 gm in 4 hours, for the patient not yet showing signs of satisfactory response another dose of 0 5 gm may be given in 4 hours The next day the patient should be given 0 1 gm 3 times a day or 3 basic doses this rate is continued until there is evidence of *satisfactory response i e slowing of pulse increase in urine output, or* loss of appetite The dose is then reduced to 0 1 gm each 24 hours If nausea develops digitalis should be stopped until the nausea disappears and then recommenced at a dose of 0 1 gm a day

For lesser degrees of congestive failure this plan can be modified in various ways In the first 24 hours 1 dose of 0 5 gm may be given followed in 4 hours by a second dose of 0 5 gm then 0 1 gm 3 times on the *second day with continuation as described in the preceding paragraph* Other plans give 0 5 gm twice in the first 24 hours with 12 hours between the 2 doses or only 0 5 gm may be given in the first 24 hours Still another plan is to begin with 0 2 gm repeated in 3 doses each 24 hours or even 0 1 gm 3 times in each 24 hours Obviously many combinations may be used A plan selected according to the degree of the patient s circulatory deficiency may work out better than a regularly prescribed one The experienced observant physician treats his cardiac patient more effectively when he does not become too dependent upon a single plan of procedure

Dosage with other of the digitalis preparations already enumerated can be determined by substituting these same multiples of the average daily dose by mouth of any one of them and proceeding on the same principles

It is to be remembered that preparations of digitoxin and digoxin have a potency 1000 times as great as that of powdered digitalis The patient must therefore be watched closely for *toxic* reactions With the increasing use of these stronger preparations failure to watch for and recognize these reactions has resulted in an increased frequency of digitalis intoxication

For the patient who has already been receiving digitalis the dosage just described should be reduced in ratio to the digitalis that has already been given and to the severity of the patient s decompensation

For the nauseated or vomiting patient or the very ill patient with marked cardiac decompensation who has not been receiving digitalis

TABLE XVI

DIGITALIS PREPARATIONS CARDIAC GLYCOSIDES

	Digitalis Leaf	*Digitoxin*	*Lanatoside C*	*Digoxin*	*Ouabain (Strophanthin G)*	*Strophanthin K*
Administered	Orally	Orally I V	Orally I.M I V	Orally I V	I V	I V
Absorption from intestine	Poor 30 to 40% in 2 hrs	Good 100%	Poor 10 to 20%	Good Nearly 100%	Poor and irregular	Poor and irregular
Speed of action orally	4 to 10 hrs Average 6 hrs	4 to 10 hrs Average 6 hrs	Irregular (Absorption poor)	1 to 2 hrs		
Speed of action intravenously						
(a) initial effect		30 min to 2 hrs	10 to 30 min	10 to 30 min	3 to 5 min	3 to 5 min
(b) maximum effect		2 to 9 hrs	2 hrs	2 hrs	30 min to 2 hrs	30 min to 2 hrs
Duration of action	2 to 3 wks	2 to 3 wks	16 to 36 hrs	24 to 36 hrs	12 to 24 hrs	12 to 24 hrs
Dose						
Usual digitalizing dose						
Orally	1 2 to 1 8 gm	1 2 to 1 8 mg	7 0 to 10 mg	2 to 4 mg		
I M			1 6 mg			
I V		1 2 to 1 8 mg	1 6 mg	1 5 mg	0 25 to 0 5 mg followed by 0 1 mg at half hour intervals until therapeutic effect	0 25 to 0 5 mg followed by 0 1 mg at half hour intervals until therapeutic effect
Daily maintenance dose						
Orally	0 1 to 0 2 gm	0 1 to 0 2 mg	1.0 mg	0 5 to 1.0 mg		
I.M			0.4 mg			
I V		0 1 to 0 2 mg	0.4 mg	0 5 mg		

digitalis and of the clinical changes to be expected following its use. Each patient should receive enough but not too much digitalis Too much is indicated by loss of appetite nausea, vomiting or diarrhea increased number of extrasystoles particularly in such number and sequence as to form a bigeminal or trigeminal pulse in the patient with a previously regular pulse rarely auricular fibrillation slowed A V conduction time and partial or complete heart block rarely disturbances of vision Of particular importance are the changes indicating slight toxicity particularly loss of appetite slight nausea diarrhea and increased extrasystoles If these appear digitalis should be stopped completely for 48 hours if only a little too much digitalis has been given, these signs will nearly disappear within this period If greater toxicity has developed then a longer time will probably be required for their disappearance After evidences of toxicity have disappeared digitalis should be given again but in smaller dosage

That enough digitalis is being given is shown by a slowing of the pulse a decrease in dyspnea a decrease in body weight and an increased flow of urine with decrease in demonstrable edema Withering expressed this well in 1795 when he wrote Let the medicine be continued until it either acts on the kidneys the stomach the pulse or the bowels let it be stopped upon the first appearance of any one of these effects When these evidences disappear begin again to give digitalis but in smaller dosage The method of trial and error remains the only way to determine how much each patient with chronic heart disease should be receiving at a given stage in the progression of his illness Recently the use of a quick acting rapidly destroyed preparation acetyl strophanthin has proved useful in determining whether patients are over- or under digitalized While the patient is continuously checked with the electrocardiogram it is given very cautiously intravenously in a dose varying from a fraction of a milligram to the full digitalizing dose of 1 2 mg depending on the state of digitalization of the patient It will immediately bring about an improvement in the patient s status or a deepening of the toxic signs depending on whether insufficient or excess digitalis is present Because of its rapid destruction and carefully controlled administration severe reactions are avoided Its use has helped considerably in selecting the proper course to follow

If *vomiting* occurs it may be the result of too little digitalis too much digitalis or an idiosyncrasy to digitalis Vomiting may be an important symptom of cardiac decompensation in some patients and if so digitalis

intravenous therapy should be substituted for the early oral dosage, 5 average daily doses of digitalis purpurea or digitalis lanata preparation in a form suitable for intravenous administration should be given once or twice during the first 24-hour period This should be followed by 1 or 2 average daily doses during each 24-hour period until the patient's condition justifies using digitalis preparations by mouth Instead of these preparations digitoxin or ouabain may be used, the average daily dose should be given intravenously each 24 hours or, rarely, 2 average daily doses at 12-hour intervals during the first 24 hour period Ouabain has the advantage of shorter duration of action than other digitalis preparations and seems preferable for intravenous use

When any drug of the digitalis group is given intravenously, greater caution must be used in patients who have previously received digitalis by mouth as the danger of digitalis intoxication is greater in these cases.

A plan useful at times for seriously decompensated patients is to give ouabain intravenously as already described and, at the same time, to give a preparation of digitalis purpurea or digitalis lanata orally at the rate of 1 average daily dose 3 times a day The effect of the ouabain will appear quickly and will last about 24 hours, during which time the more slowly acting digitalis begins to take effect

In the experience of the authors actually very few patients with chronic non valvular heart disease require intravenous digitalis medication The plan for mouth dosage described above has proved effective for the great majority of these patients When it has not been effective, in most cases it has seemed that the patients had reached the stage of their disease in which no form of digitalis therapy, including intravenous would any longer give satisfactory results

Successful therapy with digitalis depends on recognition of the fact that all patients do not have the same susceptibility to the drug The physician who adheres closely to any fixed formula of dosage will encounter some patients who exhibit toxic manifestations from it and some patients who fail to give a satisfactory response For the first group the formula of dosage contains too much digitalis for the last group too little digitalis It is obvious then that the patient receiving digitalis needs careful supervision until the physician discovers his patient's susceptibility to the drug When this has been determined, any formula of dosage in accord with it can be followed, with results that will usually be satisfactory

The procedure of giving digitalis to the patient with chronic cardiac disease should be based on a knowledge of the pharmacological action of

other diuretic drugs is needed in addition to digitalis The diuretic may be given after digitalis has had time to produce some of its effects, or it may be commenced when digitalis is begun If there is marked edema the latter plan is preferable. Increasingly diuretics particularly the mercurials are being given together with digitalis as the preferred plan of treatment

Of the diuretics the mercurials are the most effective but not necessarily and always the most advantageous Most of the mercurials should be given intravenously or intramuscularly the intramuscular route is much more desirable and is less likely to produce a serious reaction The usual dose for patients with considerable edema is 1 to 2 cc of the solution as dispensed for parenteral use With intravenous dosage it is advisable if there is no cause for great haste to bring about diuresis to give a test dose of ½ cc the day before the therapeutic dose to find out if the patient has any special susceptibility as infrequently is the case For many patients a 1 cc dose is effective others need 2 cc a rare patient requires 3 or even 4 cc Sometimes with many repetitions a patient needs gradual increase in the dose formerly effective At present mercurophylline U S P (Mercuzanthin) meralluride sodium U S P (Mercuhydrin) mersalyl and theophylline U S P (Salyrgan) and mercaptomerin (Thiomerin) are in common use Meralluride sodium and mercaptomerin are the most satisfactory since they are less irritating on injection Mercaptomerin (Thiomerin) in which sufhydril replaces theophylline is effective and not irritating when given subcutaneously Mercurial diuretics should be given often enough to remove excess fluid and maintain the patient at his normal weight This may necessitate daily injections of the diuretic or injections every other day bi weekly weekly et cetera depending on the needs of the individual patient A common error is the opinion that edema should be eliminated quickly this in turn can cause serious electrolyte disturbances The edema usually develops slowly and haste in its elimination is rarely necessary It is better for the patient to get rid of edema gradually Dosage should be guided by weighing the patient daily A continuous weight loss of a few pounds daily is preferable to a massive diuresis with a corresponding immediate weight loss of 5 or 10 pounds Such severe diuresis leads to a rapid depletion of sodium chloride potassium and calcium and can produce symptoms associated with the loss of these important electrolytes Furthermore thromboembolic complications may result

is needed in considerable amount and should be given intravenously while the vomiting continues

If digitalis is being given and nausea and vomiting result, too much digitalis is usually the cause and it should be completely stopped until the symptoms disappear This is a toxic reaction to the drug and will continue whatever route of administration is used, usually it is a central nervous system reaction and not a reaction of the gastric mucosa to digitalis in the stomach Occasionally a situation arises where the patient is vomiting, and more digitalis is needed It should then be given intravenously or intramuscularly

Rarely this reaction is the result of an idiosyncrasy to the taste of digitalis still more rarely it is caused by hypersusceptibility to the drug In the case of the former it is merely the taste of digitalis that causes nausea and vomiting is unusual, although it occasionally occurs If digitalis is made into an enteric-coated pill, it can be given orally without nausea to these patients There will also be no nausea in these cases if the digitalis is given intramuscularly intravenously, or by rectum In patients hypersusceptible to digitalis even a small dose will cause toxic symptoms including nausea and vomiting It is fortunate that this is an extremely rare reaction, as these patients must be treated without the full benefit of digitalis Usually mercurial diuretics can be used with great benefit in these cases

Quinidine The use of quinidine, as described under the treatment of arrhythmias is appropriate if an arrhythmia amenable to its action occurs and is disturbing Auricular fibrillation is of frequent occurrence in patients with chronic heart disease but it usually appears late in the course of the disease and is not appreciably influenced by quinidine For the great majority of these patients quinidine should not be given, the authors have had occasion to use it only rarely in chronic non valvular heart diseases since digitalis usually controls the heart rate and then the auricular fibrillation is not disturbing to the patient

Procaine Amide (Pronestyl) This drug may also be used as described under treatment of arrhythmias if ventricular extrasystoles are causing symptoms

Potassium chloride is useful when given in a dose of 2 to 4 gm daily for the treatment of toxic arrhythmias occurring during the use of digitalis especially if there is a low serum potassium

Diuretics For some cardiac patients with the edema of congestive failure digitalis alone is an effective diuretic For many others one of the

schedule can be determined for each patient by observing the time interval between giving the diuretic and the period at which urination becomes most frequent

Mechanical Removal of Fluid Ascites in these patients is usually controlled by diuretic drugs If not removal by abdominal paracentesis is advisable Hydrothorax is not as a rule satisfactorily controlled by diuretics If it is present in amount sufficient to embarrass respiration, mechanical removal of the accumulation of pleural fluid by thoracentesis is advised this should be done promptly and repeated as often as the hydrothorax returns to impede respiration For the patient with congestive failure and marked edema with hydrothorax the authors have always removed the hydrothorax as soon as the patient is in bed in a semi reclining position while at the same time starting digitalis therapy It is not wise to delay thoracentesis in these patients

If there is marked edema of the lower extremities rising to the level of the abdominal wall and greatly swelling the genitalia and if diuresis lags drainage with *Southey's tubes* inserted in the skin of the top of the foot is very useful It is surprising how much fluid may be drained off in this way even from the high levels of its accumulation and how rarely infection of the skin and subcutaneous tissue occurs If an infection does occur it may be controlled by the proper antibiotic

Patients from whom much fluid is being removed by either diuretic drugs or mechanical drainage will become dehydrated and so will need more fluid by mouth Since they are losing sodium and chloride they will tolerate a considerable increase in fluid intake Sometimes, but not often so much sodium chloride is lost that the patient must be given additional amounts

Cation Exchange Resins In recent years the cation exchange resins have shown promise in the treatment of heart failure because of their ability to remove ingested sodium Through their use larger amounts of sodium can be taken in the diet without the sodium being absorbed and thus increasing fluid retention and consequent edema

The sulfonate and carboxyl resins are satisfactory for oral use and effectively reduce the absorption of sodium from the gastro-intestinal tract

A mixture of potassium and ammonium carboxylated resin (Resodec) is given orally in a dose of 25 to 100 gm daily Usually a dose of 15 gm is given 3 or 4 times a day with meals and at bedtime Fruit juices such as grapefruit juice are most helpful in improving the palatability

Mersalyl and theophylline tablets U S P (Enteric Coated Tablets Salyrgan Theophylline), Enteric coated Tablets of Mercuhydrin with Ascorbic Acid), and enteric coated tablets of mercurophylline (Mercuzanthin) are suitable for mouth dosage For some patients they are effective by this route after trial to find out the most effective dosage for the individual patient For most patients, however, oral dosage of mercurial diuretics remains unsatisfactory, often causing diarrhea

A better diuresis is often obtained if, on the 2 days before administration of the mercurial diuretic, ammonium chloride, 1 to 2 gm 4 times a day after meals is given by mouth Ammonium chloride should usually be given before the administration of a mercurial diuretic Generally it is satisfactory to give the diuretic with at least a 3 day interval between doses Sometimes continuation of ammonium chloride in the dose given above without any other diuretic is satisfactorily effective It should be given as enteric-coated tablets in order to avoid stomach irritation When given in this manner, however it may not be thoroughly absorbed, but in general this is not a serious handicap

Xanthine diuretics are also available They have the advantage of effectiveness when given by mouth, and they can be given more comfortably at more frequent intervals than the mercurial diuretics with dosage planned so as to produce a more prolonged and continuing diuresis This is desirable when it can be accomplished In the experience of the authors xanthine diuretics have often given good results in the edema of chronic heart disease

Of the xanthine diuretics satisfactory results can be obtained with theobromine and sodium acetate, theobromine and calcium salicylate (Theocalcin) theophylline (Theocin) and theophylline and sodium acetate The usual dose of the theobromine preparations is 0 5 to 1 0 gm after meals 3 times a day and of the theophylline diuretics 0 1 to 0 2 gm after meals 3 times a day In general the theophylline drugs are more effective than the theobromines but are more likely to cause nausea

Urea in large doses 60 to 90 gm per day is a satisfactory diuretic for an occasional patient Its advantage is that it may be given daily to produce a continuing diuresis Its disadvantage is that for most patients it is very unpalatable its disagreeable taste can be modified by giving it in tomato or fruit juice It should be used with caution in the presence of nitrogen retention

All diuretics should be given so as to produce the maximum diuresis during daylight hours and hinder night sleep as little as possible This

Continuation Treatment after Cardiac Decompensation or Congestive Failure Has Had Effective Management

Physical activity must be arranged according to the efficiency of the patient's circulation This must be judged by observing the effects of a gradually increased period out of bed followed by a gradual increase in physical exertion For this the pulse rate can be an excellent guide Much can be accomplished for the patient's physical comfort and morale by intelligent planning of his daily life with the necessary rest periods and long hours in bed at night A plan of continuation digitalis and diuretics optimum for the individual patient must be worked out, based on his weight, the goal is to maintain this at the level obtained in the plan of treatment already described a weight termed by Gold and his associates as dry weight Diet must continue to be adequate in calories and vitamins easily digestible not bulky not excessive in carbohydrates fats, or protein the amount and content must be planned so that the patient does not get too heavy

In many respects this is the most important period of management of the patient who has undergone congestive failure with either partial or full recovery for this period makes up most of the remainder of the patient's life It is surprising how often under wise guidance this time can be lived in comfort with the patient capable of maintaining both his morale and considerable effectiveness in his chosen activities

Continuation Digitalis The patient after a successful treatment of his congestive failure should have a daily ration of digitalis This may need to range from 0 025 to 0 2 gm of powdered digitalis or 0 025 to 0 2 mg of digitoxin once a day, a rare patient tolerates and apparently needs 0 1 gm of digitalis or 0 1 mg of digitoxin 3 times a day The majority of patients do best on 0 1 gm of digitalis or 0 1 mg of digitoxin once a day but the optimum dosage should be determined for each patient by trial and error The recommended method is to have the patient take 0 1 gm of powdered digitalis or 0 1 mg of digitoxin daily until some loss of appetite develops or if this does not develop to continue the dosage for a period of 3 weeks If appetite loss appears the digitalis should be discontinued for 2 or 3 days and then given again in a smaller dose for another trial period If in the full 3 week period no loss of appetite develops a somewhat larger dose should be tried The weight of the patient observed at frequent intervals is also an important check on the plan of treatment since a rapid rise in weight indicates that edema is developing and this calls for increase in digitalis dosage

The resin should be given for 3 or 4 days and then withheld for 3 or 4 days With the added potassium the danger of a hypokalemia is avoided. Other cation electrolytes can be removed, however, and hypocalcemia may occur

Resins are not effective in removing already absorbed sodium, they are unpalatable many patients cannot tolerate them, and they must not be used if there is severe renal impairment The blood urea nitrogen and carbon dioxide combining power should be followed, and if they show changes a low-sodium syndrome or acidosis may be present and the resin should be stopped immediately

Dyspnea and *cyanosis*, if prominent, are best treated by oxygen *Oxygen* by mask should be given often in the management of the badly decompensated cardiac patient This method is preferable to giving it by a nasal catheter either in the nose or beyond the larynx, since uncomfortable dryness of the mucosa results With very marked cyanosis, particularly when there is coincident polycythemia, *bleeding* should be carried out with the removal of 250 to possibly 750 cc of blood as a therapeutic measure The best indications for phlebotomy in the treatment of congestive heart failure either acute or chronic pulmonary edema are (1) hypertension, or adequate blood pressure, not low blood pressure (2) increased venous pressure as manifested by distended neck veins with the patient sitting up, and (3) normal or reasonably normal red blood cell count and no anemia Further, for dyspnea, particularly nocturnal dyspnea, an aminophylline suppository, 0 5 gm, inserted rectally at bedtime is very useful

Acute pulmonary edema may develop abruptly It should be treated promptly by a hypodermic of 15 mg of morphine sulfate and by bleeding, with removal of 250 to 300 cc of blood unless the patient is very anemic Leg tourniquets tight enough to stop venous flow may be substituted for bleeding Tourniquets may be tried when low blood pressure or anemia contraindicate phlebotomy The tourniquets should be applied on 3 of the 4 extremities and every 15 minutes one is to be released and applied on the limb that has been free Unnecessarily prolonged application is not advised for thrombophlebitis and embolism may result Oxygen also should be used given by mask

Intravenous aminophylline in a dose of 0 5 to 1 0 gm also may be very effective In many of these patients rapid digitalization is indicated if it has not been carried out already and a mercurial diuretic should be given Atropine which is frequently given probably has very little influence on the acute pulmonary edema of chronic heart disease

sible Frequent weighing of the patient is the most satisfactory way to determine the effectiveness of diuretics

In some instances where continuation of diuretics is required, the edema may remain most obstinate This may result from electrolyte imbalance due to the too frequent use of diuretics such as a mercurial diuretic given daily In such cases the diuretic should be withheld for 2 or 3 days and ammonium chloride as a palatable syrup 0 5 gm in 4 cc given in a dose of 1 0 gm 4 to 6 times a day for 3 days prior to mercurial injection Another method of obtaining improved disuresis in such intractable cases is by the use of aminophylline, a potentiator The patient may be given a parenteral mercurial diuretic, such as 2 0 cc mercuhydrin intramuscularly or thiomerin 2 0 cc subcutaneously or with less likeli hood of irritation, intramuscularly and 30 minutes later 0 5 gm amino phyllin is given *very slowly* intravenously

Oral Diuretics Recently several oral diuretics have been found to be effective for continuation diuresis An oral mercurial, chlormerodrin (Neohydrin) can be given daily, or every few days to aid in control of mild edema It may be used also as a supplement to parenteral injection of mercurial diuretics to prolong the edema free period Each tablet dosage is 18 3 mg (equivalent to 10 mg mercury) and for best results 2 or 3 tablets should be given in the morning after breakfast

Acetazoleamide (Diamox) related chemically to the sulfonamides acts as an oral diuretic through supression of the enzyme carbonic anhydrase in the renal tubules This leads to a loss of bicarbonate ion which in turn carries out sodium, potassium and water producing an alkaline urine and diuresis Acetazoleamide may be used effectively in the treat ment of hyperpotassemia particularly when it results from transfusion of incompatible blood, unless there is massive impairment of the kidneys In large doses it may produce side effects of drowsiness and mild pares thesias tingling of finger tips and around the mouth The usual dose of acetazoleamide is 5 mg per kilo of body weight, approximately one 250 mg tablet in the morning It may be used intravenously, 250 mg dissolved in 2 5 ml of sterile isotonic sodium chloride As the drug produces a mild acidosis it should be used with caution in cases of existing metabolic acidosis Acetazoleamide is contra indicated in patients with idiopathic renal hyperchloremic acidosis, in those who have had severe loss of sodium or potassium and in cases with Addison s disease

Another recent non mercurial oral diuretic is a brand of aminoiso metradine (Rolicton) With little or no effect on glomerular filtration

or the use of a diuretic in addition to the digitalis In this way the optimum dosage for the individual patient can be determined

There is a rare patient for whom 0 025 gm of powdered digitalis daily is optimum, a considerable number of patients for whom 0 05 gm daily is optimum, very many for whom 0 1 gm daily is optimum, and a considerable number for whom more than 0 1 daily is optimum There are many patients for whom the optimum dosage is between the ones just enumerated For them, for example, alternate a smaller and a larger dose, such as 0 05 gm one day and 0 1 gm the next, or give the digitalis preparation every other day or 4 or 5 days out of the week By such trial and error method the physician can arrive at the dosage that is most suitable for each patient and that produces the best results for continuation digitalis therapy

Continuation digitalis is in the opinion of the authors desirable also for the patient with evidences of chronic non-valvular heart disease who has never had congestive failure but who has very slight evidences of cardiac insufficiency, and also for the patient with enlarged heart and no symptoms of cardiac insufficiency

Continuation Diuretics For many patients continuing or recurring edema is an unpleasant feature of otherwise moderate cardiac insufficiency For this the various diuretics, already described, may be used Again, the trial and-error method is advised Any of the diuretics described in a previous section may be used Diuretics by mouth may be tried first ammonium chloride one of the xanthines or a mercurial. Since ammonium chloride must be given several times each day, has a tendency to produce nausea and on long use acidosis, and even then is only moderately effective it does not often prove satisfactory Many more patients find a xanthine or mercurial diuretic by mouth effective usually these should be given every second or third day preceded by ammonium chloride If they do not prove satisfactory, a mercurial diuretic given intramuscularly once or twice a week (or even more frequently) is often effective Many patients have benefitted from this treatment for many weeks with dosage guided by frequent weighings and the diuretic increased when weight gain indicated returning edema

The physician has a considerable number of diuretics from which to choose Many variations in size of dose and in repetition and route of dosage are available Consequently from many plans of treatment one that best suits the individual patient may be selected The goal in using continuation diuretics is to keep the patient as free from edema as pos

penicillin combined, as needed, with therapy for chronic heart disease Also in this group are cases of chronic valvular heart disease complicated by bacterial endocarditis at some stage in their progression, in which the injurious effects of the bacterial lesion can be ameliorated or stopped by the use of antibiotics, especially penicillin After the use of penicillin in these patients the usual progression of a chronic valve lesion can be expected unless bacterial endocarditis recurs and speeds it up, treatment then will be just as if the bacterial endocarditis had not occurred, except that when antibiotic therapy is not used in the early stages of the bacterial endocarditis there will be an additional valve lesion from either the destructive or the fibrosing action of the bacterial endocarditis

Chronic Heart Disease Complicated by Various Forms of Arrhythmia As a rule, when arrhythmias develop in the course of the progression of chronic heart disease the treatment described for them should be instituted as a supplement to that already being carried out for the preexisting chronic heart disease Often the arryhythmia needs no special treatment This is particularly true of auricular fibrillation, which occurs frequently in the progression of chronic heart disease quinidine should not be given in an effort to stop it unless the fibrillation antedated and probably caused the decompensation Digitalis is capable of controlling the fast heart rate of this arrhythmia

Management When Cardiac Therapy Begins to Fail

Unfortunately the progression of chronic heart disease, although it may be slowed can be expected in most patients to be fatal. This being so, a stage will be reached in which cardiac therapy is no longer effective Dosage of digitalis can be increased only until toxicity contraindicates it, diuretics too will eventually lose their effectiveness Excess edema now can be removed only by mechanical methods For the patient the time has come when continued bed or chair life is the only possibility The physician must use methods of treatment modified to suit the limitations of the patient and carried out so as to cause him the least possible discomfort A sympathetic but cheerful physician can do much to maintain patient morale Many previously important restrictions can now be relaxed There are many things that a cardiac patient can do in bed or chair to interest him and help to pass the time A good nurse is important in fact practically indispensable At this stage sedation should be increased to give the patient a maximum of comfortable

rate, renal plasma flow, cardiac output, heart rate, and blood pressure, its effectiveness is thought to be due to inhibiting reabsorption of sodium ions by the renal tubules Aminoisometradine is well tolerated when given with meals It may cause headache or mild gastro-intestinal symptoms, such as anorexia and nausea Aminoisometradine, 400 mg may be given 4 times daily for one day and then 2 times a day to maintain an edema free state It exerts a continuing diuretic effect.

Modifications of Treatment for Special Forms of Chronic Heart Disease (Reversible Heart Disease)

Chronic Heart Diseases Amenable to Surgery There are some forms of chronic heart disease in which the lesion chiefly causative of the cardiac disability can be corrected by surgical methods For the most part, the treatment outlined in the previous pages need no longer be applied at all, or need be applied only in a modified form according to the circulatory insufficiency remaining after convalescence from the surgical operation Notable examples of this type are the various forms of congenital heart disease that are amenable to surgery

Another example of chronic heart disease to which surgical treatment should be applied is constrictive pericarditis Still another is arteriovenous aneurism, in which much, if not all, the cardiac disability will disappear after the arteriovenous aneurism has been excised or effectively ligated

Brilliant results are now also being obtained by surgical enlargement of stenosed mitral valves, whereby the calcified leaflets are fractured and the opening made more patent

Sympathectomy, when successful, will reduce hypertension and the cardiac hypertrophy and insufficiency resulting from it

The heart disease of thyrotoxicosis with hypermetabolism is amenable to thyroidectomy if medical therapy does not control it, except in cases where the cardiac lesion has become irreversible Before thyroidectomy, patients with cardiac decompensation should have therapy with iodides and propylthiouracil until the basal metabolism approaches normal

Chronic Heart Diseases Amenable to Treatment Directed against an Infectious Etiology This group is of increasing importance since the development of satisfactorily effective antibiotics Syphilitic aortitis and aortic insufficiency are now more satisfactorily treated by the use of

13 VANDERVEER J B CLARK T W and MARSHALL I S Prolonged Use of Oral Mercurial Diuretics in Ambulatory Patients with Congestive Heart Failure *Circulation*, 1950 I p 516

14 VOGL A and ESSERMAN P Aminophyllin as Supplement to Mercurial Diuretics *Jour Amer Med Assoc*, 1951 CXLVII p 625

15 SCHNITKER, M A *Congenital Anomalies of the Heart and Great Vessels* Oxford University Press New York, 1952

hours and as much sleep at night as possible, whether in bed or propped up in a large, pillowed chair with an adjustable foot rest Often patients rest more comfortably in a chair at this stage of the disease Morphine usually works best as a sedative, given in repeated doses of 5 to 10 mg, its use is advised now without consideration of its habit-forming propensities

BIBLIOGRAPHY

1 ARNOLD W P JR 'Medical Uses of Ion exchange Resins,' *N E J Med*, 1951 CCXLV p 331
CHRISTIAN, H A *The Diagnosis and Treatment of Diseases of the Heart*, Oxford Univ Press 1940
3 CITRON D BERCU, B LEMMER, R and MASSIE, E Congestive Heart Failure and Hyponatremia Untoward Effects of Mercurial Diuresis,' *Ann Int Med*, 1951 XXXIV, p 872
4 DeGRAFF A C Modern Management of Heart Disease' *Jour Amer Med Assoc*, 1948 CXXXVI p 10.5
5 ENSELBERG C D and SIMMONS H G Clinical Experience with Thiomerin Observations on Its Use in 205 Patients," *Am Jour Med Sc*, 1950 CCXIX p 130
6 GOLD H, KWIT N T MODELL, W HANLON L W, KRAMER M GREENBERG S, OTTO, K. L, COTLOVE, E W BENTON J G PEARLMUTTER, M and ZAHM W System of Routine Treatment of the Failing Heart, *Am J Med*, 1947 III p 665
7 ISERI L T BOYLE A J and MYERS G B Water and Electrolyte Balance During Recovery from Severe Congestive Failure on a 50 mgm Sodium Diet, *Am Heart Jour*, 1950 XL, p 706
8 JUDSON W E Present day Treatment of Congestive Heart Failure' *Med Clin No Amer*, Sept. 1951 p 1333
9 LEVINE S A The Myth of Bed Rest in the Treatment of Heart Disease *Am Heart Jour*, 1951 XLII, p 406
10 MARVEL R J and SHULLENBERGER, W A Thromboembolic Phenomena Associated with Rapid Diuresis in the Treatment of Congestive Heart Failure *Am Heart Jour*, 1951, XLII, p 194
11 OVERMAN W J GORDON, W H, JR and BURCH G E Tracer Studies of Urinary Excretion of Radioactive Mercury Following Oral Administration of Mercurial Diuretic' *Circulation*, 1950 I p 496
12 STEWART H J, McCOY H I SHEPARD, E. M and LUCKEY E. H Experience with Thiomerin New Mercurial Diuretic *Circulation*, 1950 I p 502

with cholesterol values higher than normal should be instructed to partake of a diet reduced in fat and cholesterol content The value of this however, remains debatable

A palatable well balanced diet that contains at least 1 gm of protein per kilogram of body weight and is rich in vitamins is recommended The salt intake should be moderate Reduction in cholesterol and fat content is recommended by some but this restriction should not be carried to the extent of making the diet unpalatable as is so often done Excessive intake of egg yolk and butter cream and other fats should be avoided Overeating heavy meals before bedtime and excessive calorie intake are to be avoided Proper regulation of calorie intake to calorie needs is important

Physical activity or exercise to the point of fatigue is unwise Heavy lifting straining at stool excessive coughing and other activities producing sudden arterial strain can be harmful Moderate exercise however, is desirable

Mental tension emotional strain worries anxiety and psychological maladjustment are harmful reassurance psychological adjustment and relief from mental stress and strain are indicated if these conditions exist Patients should be taught to relax to take a more calm view of life and to avoid emotional turmoil Psychiatric advice often proves most helpful in the tense introverted compulsive type of individual

Tobacco consumption should be restricted When taken in excess alcohol in all forms is harmful A small amount taken at mealtime is not harmful and may prove beneficial

Many advocate the use of the iodides vitamin B complex vitamins lecithin and choline as agents of value in helping metabolize or mechanically disperse absorbed fat and cholesterol Although these have been shown to be effective in experimental animals, it is doubtful if they are of any real value in most patients with arteriosclerosis

Potassium iodide given as a saturated solution in a dose of 10 drops in milk or fruit juice 3 times a day may be tried The vitamin B complex intake should be increased so that the patient receives approximately 5 times the normal daily requirement This therapy is of more value if there is an associated diabetes mellitus with a possible deficiency in the vitamins of the B complex

ARTERIAL ANEURISM

The treatment of aneurism is still unsatisfactory although recent ad

CHAPTER LXIII

DISEASES OF THE ARTERIES

For treatment purposes diseases of the arteries may be considered as originating from congenital defects, degenerative lesions functional abnormalities, inflammation trauma, and various combinations of these The treatment of congenital defects is discussed under Congenital Heart Disease

Arterial Degenerative Disease

Arteriosclerotic degeneration of arteries produces many clinical syndromes requiring therapeutic measures other than those directed primarily against the arteriosclerosis Measures taken to ameliorate and perhaps prevent further development of arteriosclerosis are, however fundamental in the management of these syndromes

Arteriosclerosis

Arteriosclerosis presents a difficult therapeutic problem There is no specific therapy available Consequently efforts must be directed toward the amelioration of the impaired function of the artery and organs or tissue supplied by it, and measures must be taken to prevent further damage

Patients showing signs of the disease especially those exhibiting symptoms of organ or tissue damage, should have the nature of the disease explained to them and should be urged to live a quiet, well regulated life avoiding excesses in food drink, and activity

Endocrine disturbances such as myxedema and hyperthyroidism are harmful and must be corrected Diabetes mellitus, if present, requires careful regulation Infections should be eliminated by prompt vigorous therapy Exposure to lead and other toxic agents is to be avoided

Obese patients require reduction in weight The loss should be gradual usually no more than 2 pounds a week since a more rapid loss of weight may be harmful

Individuals exhibiting difficulty in metabolizing cholesterol and those

of the acute attacks and measures employed to avoid recurrence and prevent further development of the underlying disease

The acute attack usually responds promptly to a nitroglycerin tablet (hypodermic tablet), 0 3 mg placed under the tongue The dose may be repeated if relief is not gained at once Amyl nitrite 0 18 cc given by inhalation is also rapidly effective in most patients The glass container is crushed in a handkerchief and the vapor inhaled Care must be taken to avoid overdosage with nitroglycerin or amyl nitrite since excessive dosages may cause collapse Usually no more than 3 or 4 doses should be taken during a 30-minute period For patients in whom nitroglycerin causes uncomfortable symptoms a glass of sherry or 1 or 2 teaspoonfuls of whiskey taken neat will often relieve anginal symptoms Prompt pressure on the carotid sinus sometimes produces immediate relief Inhalation of oxygen also is helpful but except for bed patients, impractical

Treatment between attacks consists of general and prophylactic measures taken to arrest development of the underlying disease and prevent future attacks Precipitating causes of attacks must be ferreted out and removed if possible The nature of the disease should be explained carefully and the patient reassured The fear of impending death present in the minds of many patients when they hear the name angina pectoris should be dispelled

Treatment as described for arteriosclerosis should be employed where applicable When daily activities cause attacks, they must be curtailed and the patient s life readjusted so as to require less stress and strain Occasionally a period of bed rest or long rest in bed on weekends or in the middle of the week is necessary Precipitating factors such as overactivity fatigue emotional and mental tension and turmoil uncontrolled anger overeating coitus obesity smoking alcoholic drinks exposure to cold infections chronic illness sympathomimetic drugs hypoglycemia anemia hemorrhages gallbladder disease digestive disorders, hyperthyroidism trauma—in fact any activity either mental or physical that results in stress or strain and more particularly precipitates attacks must be ameliorated avoided or treated as effectively as possible When a precipitating cause cannot be avoided a small dose of nitroglycerin given before the activity will often prevent the attack

If the exciting cause is not readily apparent it is necessary to make a careful study of the patient s daily activities to discover if possible the precipitating factor or factors. If hypertension hyperthyroidism or syphilis is present treatment for these diseases is essential

vances in surgical technique give hope that more effective measures will be available in the future for thoracic and abdominal aneurisms Those on peripheral vessels, if causing symptoms, can and should be treated by surgical measures, including excision when collateral circulation is adequate Cerebral aneurisms should be attacked surgically if possible

Mycotic aneurisms no longer carry a hopeless prognosis Treatment with the proper antibiotic will result in a high percentage of cures and will prevent further damage to vessels by the infecting organism Antibiotic therapy, as described for Subacute Bacterial Endocarditis is recommended

Dissecting intrathoracic and intra abdominal aneurisms require absolute bed rest and avoidance of all exertion during the acute phase Morphine sulfate, 15 mg given subcutaneously and repeated at 3 to 4-hour intervals as required for relief of pain, is indicated Meperidine (Demerol), hydrochloride, 100 mg intramuscularly at 3- to 4 hour intervals, is also helpful and may be used instead of morphine when sedation is not desired

Following the acute episode, treatment should consist of bed rest and gradual resumption of activities, as described for Coronary Occlusion

Arteriosclerotic Aneurisms and Aortic Arteriosclerosis

Arteriosclerotic lesions of the aorta producing aneurisms, dilatation or tortuosity may or may not cause symptoms requiring treatment When anginal pain, aneurismal pain, hypertension, or myocardial insufficiency exist, treatment as described for arteriosclerosis is recommended, together with the therapy advised for the specific complication Aneurisms should be evaluated thoroughly and possibly subjected to surgical repair measures Recent surgical advances revive hope that more effective treatment of aneurism can be expected Syphilitic aneurisms are discussed under Syphilis Surgery can be tried in some cases

Coronary Arterial Arteriosclerosis

Arteriosclerosis of the coronary arteries may either remain asymptomatic or produce angina pectoris coronary artery insufficiency or coronary artery occlusion with myocardial infarction of varying degrees

Angina Pectoris

The treatment of this painful syndrome is divided into management

the drug should be discontinued for 2 or 3 days and then a lower dosage level established

Papaverine hydrochloride, 30 to 80 mg by mouth 3 times a day, is sometimes helpful especially when anginal attacks are precipitated *secondarily by pain or spasm from the gastro intestinal* tract, gall bladder or genito urinary tract Since papaverine can be obtained from opium it is subject to the narcotic laws and can only be dispensed *subject to these regulations*

Dioxyline (Paveril) phosphate has a therapeutic action similar to that of papaverine and is thought to have a wider margin of therapeutic usefulness It is not subject to the narcotic laws and can be used when a papaverine like action is desirable A dose of 200 mg 3 times a day is recommended

Frequently recurring attacks (status anginosus) are serious and usually foreshadow a coronary occlusion Since the attacks probably *signify myocardial infarction the patient should be treated as described* for that disease

Patients with angina pectoris are likely to develop a coronary occlusion Consequently great care must be taken to see that their angina is adequately managed in the hope that collateral circulation will develop in sufficient degree to permit a more normal existence Repeated electrocardiograms are helpful in properly evaluating the status of these patients With proper management coronary occlusion and myocardial infarction can often be *prevented or their effects* minimized

Severe intractable anginal pain may prove incapacitating Occasionally it is *necessary to eliminate* this pain in order to relieve the patient Various surgical measures have been employed with considerable success Cervico-thoracic ganglionectomy by posterior spinal root division paravertebral alcoholic injection of the sympathetic cord its rami and the intercostal nerves and possibly surgical measures to increase blood supply to the myocardium *such as grafting muscle to the heart* have proved of value as have such measures as thyroidectomy treatment with radioactive iodine and with propylthiouracil which reduce the tissues *demand for oxygen and consequently reduce the work of the heart* Unfortunately all of these measures have drawbacks some of serious degree which limit their usefulness possibly the most serious is the loss of warning previously given when the heart was under increased stress although many minimize the importance of this Thyroidectomy unfor-

Prophylactic drug therapy has not proved very satisfactory Occasionally, tense, nervous, emotionally unstable, and overactive patients may be afforded relief by mild sedation if these conditions cannot be removed by a psychological approach Phenobarbital, 15 mg 3 or 4 times a day is recommended Sometimes, but not often, it proves helpful when hypertension is a complicating factor Unfortunately sedation is too often overused in these patients For most patients, especially the older ones it is better not to use a barbiturate sedative

If myocardial insufficiency is a complicating factor relief of congestive failure by the use of digitalis, mercurial diuretics and a salt restricted diet as described for congestive failure is indicated and may prove helpful in preventing attacks

Quinidine sulfate, 0 2 gm 3 or 4 times a day by mouth, or procaine amide (Pronestyl) hydrochloride 0 5 gm every 4 hours by mouth, is occasionally effective in preventing attacks produced by aberrant rhythms

Opinion is divided on the value of xanthines in the therapy of angina pectoris They are worthy of trial and occasionally give excellent results Theophylline ethylenediamine (Aminophylline) is the most effective xanthine, and when given in a dose of 0 5 gm as suppositories by rectum or 0 1 to 0 2 gm as enteric-coated tablets by mouth 2 or 3 times a day it sometimes affords considerable relief The rectal route is the most effective

Mannitol hexanitrate, 16 to 32 mg every 4 to 6 hours, is frequently of temporary help in preventing attacks Long continued use of this drug, however leads to anemia methemoglobinemia, and headaches while at the same time the drug becomes less and less effective

Pentaerythritol tetranitrate (Peritrate), like mannitol hexanitrate, is a long-acting nitrate that exhibits an ameliorating effect on angina pain It is given in a dose of 10 mg 3 or 4 times a day Occasionally 20 mg 3 or 4 times a day are required for best effect Results with this drug are encouraging but what has been said about the toxic effects of mannitol hexanitrate is probably true also of this drug

Khellin (Eskel) may also be helpful in some patients in relieving repeated painful angina attacks It is given by mouth and the dose should be adjusted to the needs of the individual patient A dose of 20 to 40 mg a day is given at first and this is gradually increased by 10 mg every 3 or 4 days until the desired therapeutic response occurs or anorexia nausea vomiting, or dizziness appears If toxic signs develop,

Oxygen is beneficial if there is dyspnea cyanosis, or shock and should be started promptly A concentration of 95 per cent given by mask, nasal inhaler, or catheter is recommended in the first few hours the mask method is preferred Subsequently a tent or hood with a flow of 8 to 12 liters per minute may be substituted If the patient becomes restless or apprehensive, the hood or tent should be removed and inhaler, mask, or catheter substituted provided these do not cause distress High concentrations are best continued 2 or 3 days and then gradually reduced Severe cases may require some oxygen for 10 days to 2 weeks It is to be realized that since such use of oxygen is frightening to most patients, it should not be used routinely but only in cases of dyspnea, cyanosis, or shock

Immediate reassurance and calmness on the part of the doctor, nurses and family are essential especially when oxygen is given Patients should be informed of the nature of the disease and their excellent chance for recovery Excitable, tense, restless patients are sometimes helped by sedation Phenobarbital, 30 mg by mouth 2 or 3 times a day, is effective if morphine is not in use Routine use of phenobarbital is undesirable

Patients in shock or developing shock are to be kept warm, the foot of the bed should be elevated and oxygen in high concentration administered Caffeine and sodium benzoate 0 5 gm intravenously, repeated in 15 minutes if necessary is helpful If pulmonary edema is not a complicating factor and systolic blood pressure is falling, citrated whole blood salt free human serum albumin, or normal human plasma given by an intravenous infusion of 250 cc over a period of 1 to 1½ hours is beneficial and may be repeated in 2 hours if necessary Intra arterial transfusions of small amounts of whole blood are also useful in critical cases if blood pressure is very low and there is some evidence of pul monary edema This serves to increase the blood pressure quickly and insure a good coronary artery supply In the occasional patient who is rapidly growing worse with a systolic blood pressure of 90 mm of mercury or less and in whom no cardiac irregularities are present, ephedrine sulfate 25 mg subcutaneously is helpful Phenylephrine (Neosynephrine) hydrochloride 10 mg subcutaneously, is likewise effective and may be given in place of ephedrine when a shorter-acting drug is desired The dose may be repeated in 3 hours if needed Norepinephrine (Levophed) bitartrate and mephentermine (Wyamine) sulfate have recently been used in the same situations with encouraging

tunately produces myxedema, which is difficult to manage and in the light of present-day knowledge actually may be harmful in that arteriosclerotic activity may be augmented The same criticism also pertains to propylthiouracil and radioactive iodine

Coronary Occlusion and Myocardial Infarcation

Management of this acute medical emergency consists of measures to control and secure relief from the acute attack and its complications, and procedures to prevent and control further development and damage from the disease

Acute Attack Immediate and absolute rest is essential For the patient who is acutely ill, particularly if he is in shock, complete bed rest should be carried out After several days, when all pain has been relieved and good pulse and blood pressure have been maintained, the physician may advise the chair treatment which is being used more and more in the therapy of acute coronary thrombosis This is more fully described on page 739

For pain that is mild or moderate in intensity, with little apprehension, give morphine sulfate, 15 mg subcutaneously, if pain continues, repeat in 2 hours giving 10 mg In the presence of severe pain, apprehension, fear or mental anguish, morphine sulfate, 15 mg intravenously is recommended Subsequent injections, if required, may be given subcutaneously, 10 to 15 mg every 4 hours The patient should be kept quite free of pain Care should be taken to avoid respiratory depression and resulting anorexia Caffeine and sodium benzoate, 0 5 gm intravenously, is helpful if respiratory depression of harmful degree develops If morphine causes too much sedation, dihydro-morphinone (Dilaudid) hydrochloride 2 or 3 mg subcutaneously or meperidine (Demerol) hydrochloride 100 mg intramuscularly may be substituted If these measures fail to relieve the patient, intravenous aminophylline, 0 5 gm, may prove helpful Give it slowly and carefully, allowing at least 5 minutes for the injection and halt if flushing, fainting, or fall in blood pressure occurs Papaverine hydrochloride, 60 mg given intravenously, occasionally may give relief when morphine and aminophylline have failed Administration should require at least 3 minutes and should be stopped at once if any of the untoward reactions, similar to aminophylline, develop

anticoagulants and generally in serious cases with congestive failure or those already showing evidence of embolic phenomena the anticoagulants should be given It must be remembered, however, that serious hemorrhages sometimes follow their use

For these reasons it is the opinion of the authors that anticoagulants should not be used routinely in treating patients who have had a coronary occlusion but that their use should be reserved for those patients in whom there is clinical evidence that a pulmonary infarct has developed and possibly for those in whom there is electrocardiographic evidence that the myocardial infarct is localized in the wall of the right ventricle instead of, or in addition to, the wall of the left ventricle also, with the appearance of congestive failure and the probability of vein thrombosis in the legs, it is recommended that anticoagulants be used Patients who can be treated satisfactorily in the home however should not be removed to the hospital for the possible benefits that might be secured from antocoagulant therapy

When anticoagulant therapy is thought advisable it is recommended that it be given in the following manner After the determination of the clotting time and prothrombin activity heparin 60 to 75 mg intravenously is given at once and repeated at approximately 4 hour intervals for 24 to 48 hours in order to maintain a clotting time of from 2 to 3 times the normal value for the patient Dicumarol, 0 2 to 0 3 gm, given by mouth in divided doses is to be commenced at the same time and continued in a dose of 0 1 to 0 2 gm daily as needed to maintain prothrombin activity between 15 and 20 per cent of normal. Heparin should be discontinued as soon as the prothrombin activity has been reduced by Dicumarol to 15 to 20 per cent of normal The initial and subsequent dose of Dicumarol is regulated by determination of prothrombin activity before administration of the drug According to some Dicumarol should be continued for 30 days, others advise using it for only 14 days there is also precedent for a continuation time between these two

The decision to give anticoagulants must be based on knowledge of the absence of conditions that in themselves lower the prothrombin level of the patient being treated Patients with liver or kidney disease nutritional deficiencies and congestive failure are more sensitive to the drug and dosage must be reduced accordingly Dicumarol is contraindicated in hemorrhagic blood dyscrasias in bleeding ulcers of the gastro intestinal tract, in the period immediately following surgery and

results When given properly, to maintain a systolic blood pressure at or slightly over 100 mm mercury, neither drug appears to cause disturbances of cardiac rhythm or to precipitate or aggravate cardiac insufficiency Nor-ephinephrine, which is supplied in ampules containing 4 mg of the bitartrate monohydrate, is to be diluted in 1000 cc of 5 per cent glucose or 0 85 per cent sodium chloride and administered intravenously through a Murphy-drip apparatus at an average maintenance rate of 20 to 30 drops per minute Mephentermine may be administered in a single dose of 5 to 20 mg intravenously, or by slow intravenous drip, 10 to 20 mg in 100 cc glucose or saline, at a rate of 1 mg per minute Mephentermine may also be given intramuscularly, 35 mg per dose, at intervals sufficient to maintain a systolic blood pressure around 100 mm mercury In the presence of any irregularity in cardiac rhythm none of these drugs is advised

Arrhythmias in the form of auricular or ventricular tachycardia, ectopic beats, heart block, and auricular fibrillation or flutter must receive prompt therapy, since they are often the first warning of an impending ventricular fibrillation Treatment for these arrhythmias is described on page 675 The routine administration of quinidine as a prophylaxis against ventricular fibrillation is not advised

Anticoagulant therapy is helpful, and many advise its routine use for a long period of time When heparin is given, it must be administered intravenously or intramuscularly, with dicumarol also it is necessary to have frequent prothrombin determinations, both drugs thus involve many venous punctures Because veins are likely to be injured in time, entering them is often difficult These frequent venous punctures become greatly dreaded by the patient, and are frequently painful The many prothrombin determinations that are needed involve much work by laboratory technicians and this is an additional heavy expense to the patient Fatal pulmonary embolism is not a frequent occurrence at least in the experience of the authors, since intracardiac thrombi appear more commonly in the left than in the right heart and so, if they escape, they go into the peripheral not the pulmonary, circulation On the other hand, an embolus to the brain can cripple an otherwise successfully treated case of coronary thrombosis

Another reason for the use of anticoagulants is to prevent further clotting of blood in the coronary vessels and possibly to soften existing clots so as to re-establish the circulation in occluded vessels There is statistical evidence of a lowered mortality following prolonged use of

tion during the first 3 or 4 days, since any increased activity at that time should be avoided

Nausea, vomiting, and retching are harmful and should be relieved promptly Chlorpromazine (Thorazine), 25 to 50 mg intramuscularly for the patient who is vomiting or the same dosage by mouth for nausea, usually is very effective Liquid Gelusil, 15 cc every 2 hours or cool drinks (not iced drinks), fruit juices, or champagne may be of value Dimenhydrinate (Dramamine) 50 mg 3 or 4 times a day, has proved useful in controlling nausea and vomiting

Bed rest for very ill patients should average from 6 to 8 weeks After the first 4 weeks limited activity is advised, such as flexing muscles, turning in bed breathing exercises and use of the commode for those who find using the bedpan and urinal difficult and annoying These activities should be gradual, and if the heart rate rises as a result they must be curtailed and gradually resumed later At the end of 6 weeks, sitting in a chair for half an hour to an hour may be permitted, this may be gradu ally increased by an additional hour each day In milder attacks these restrictions should be reduced

For patients not so severely ill a less strict bed regime is advised If pain ends quickly and if dyspnea is not present, this 6 week period of bed rest can and should be materially shortened in the opinion of the authors Many patients need only two weeks in bed, others more To determine this requires a wise clinical summarizing of the patient s condition For many patients an earlier and more rapid return to some physical activity is permissible Recent experience has shown that patients given their rest during the day in a chair do very well This is especially true if there is any element of cardiac decompensation because the recumbent position favors the development of pulmonary congestion and edema, thereby increasing the work of the heart, while the erect position through the action of gravity lessens pulmonary congestion and with it cardiac effort In other words it is better to have the congestion and edema in the legs and lower part of the body, where they can cause no harm than to have them in the lungs and upper portion of the body where they cause symptoms and increase cardiac work Patients selected for chair rest should be eased carefully into the chair and should remain there quietly for several hours each day This should be started as soon as the acute episode has subsided Care must be taken to avoid undue exertion in getting patients in and out of the chair Skilful nursing care is essential Every effort must be made to

in severe renal or liver impairment Should hemorrhage occur, immediate injection of vitamin K_1 oxide 60 to 100 mg, given slowly intravenously and repeated at 6- to 12-hour intervals as needed, is recommended Anti coagulant therapy should be continued for at least 3 to 6 weeks, longer if thrombo embolic phenomena appear

Congestive heart failure and pulmonary edema, when present, should be promptly corrected Care must be taken, however, in the use of digitalis and other cardiac glycosides, since their irritant effect on the myocardium can produce dangerous arrhythmias When indicated by definite signs of cardiac failure, digitalis should be given cautiously, and care should be taken to avoid toxic effects Usually digitalization requires 24 to 36 hours when used after acute myocardial infarction Routine use of digitalis in patients with myocardial infarction is not advised because of a possible resultant serious ventricular arrhythmia Fortunately congestive failure is infrequent in these patients and consequently digitalis is not needed The finding of a few rales at the lung bases after an acute coronary occlusion is frequent and in itself does not call for the institution of digitalis therapy Only when there is more evidence than this of cardiac insufficiency should the use of digitalis be considered

General care of the patient should include cheerful, helpful nursing attention careful observation of day-to day progress, and measures to avoid mental tension and unrest during the long period of bed or chair confinement required

The diet for the first few days after the acute attack should be largely liquid in the form of milk, eggnogs, broth, and sweetened fruit juices For the first few days the patient should be fed The volume permitted at a feeding should not be excessive, 250 to 300 cc '4 times a day is satisfactory This is to be followed by a bland diet consisting of 1200 to 1500 calories and sufficient liquids to satisfy the patient's desires Ice water should not be permitted It should contain ample vitamins Vitamin B_1, 10 mg daily by mouth, is recommended for patients likely to have or already exhibiting vitamin B deficiency

The use of tobacco should be discontinued Patients may have wine, brandy, or whiskey with meals, if they so desire

Constipation must be prevented, or relieved promptly if present Milk of magnesia, 15 to 30 cc by mouth, or cascara sagrada, 0 3 to 0 6 gm, is recommended Occasionally it is necessary to give a soapsuds enema in order to secure relief No effort should be made to relieve constipa

its necessity) the substitution of small amounts of wine brandy, or whiskey at mealtimes often is helpful

Postural exercises (Buerger's exercises) as described for thrombo angiitis obliterans are useful and should be carried out—at least they do no harm Mechanical intermittent venous occlusion machines, oscillating beds, and suction pressure boots occasionally are helpful, but it is doubtful whether the benefit gained warrants the use of such cumbersome and expensive devices

Warm Sitz baths at body temperature promote circulation and are helpful If there is no ulceration infection, or gangrene, foot baths of warm boric acid solution, 100° F, morning and evening are useful in preventing foot infection and increasing circulation

Many drugs have been used with varying degrees of success in attempts to promote increased circulation None of them, however, is entirely satisfactory, and in older patients unfortunately unfavorable side reactions develop all too frequently In such patients unless there is obvious circulatory inefficiency these drugs should not be used Papaverine hydrochloride 30 to 60 mg by mouth 3 or 4 times a day, benzazoline (Priscoline) hydrochloride, 25 to 50 mg by mouth 5 to 6 times a day, deproteinated pancreatic extract (Depropanex) 2 to 3 cc tetraethyl ammonium (Etamon) chloride 10 cc given with caution once daily, nicotinic acid alcohol (Roniacol) tartrate 50 to 100 mg 3 or 4 times a day, or 5 per cent sodium chloride solution 100 to 200 cc intravenously once a week may be tried A recently introduced sympathetic blocking agent, Dibenzyline in a dose of 10 to 20 mg 4 to 6 times a day shows promise especially in those patients who are found to have sympathetic induced vasospasm

If pain is troublesome, acetylsalicylic acid 0 3 to 0 6 gm by mouth 2 or 3 times a day is helpful More severe pain may require codeine phosphate 30 to 60 mg for relief Cramps at night are at times relieved by having the patient take a deep breath and hold it They may often be prevented by quinine sulfate, 0 3 to 0 6 gm by mouth at bedtime

If skin temperature tests show a definite element of vasospasm sympathetic neurectomy performed by a surgeon skilled in the technique is often most helpful

Thrombosis of an arteriosclerotic artery should be treated by anticoagulant therapy with heparin 10 cc of a 1 per cent solution intravenously, followed immediately by Dicumarol as described for coronary occlusion The involved limb should be protected from circulatory

keep the patient from making any greater effort during feeding, elimination, and other medical or nursing procedures than would be ordinarily required on strict bed rest Patients on this chair-rest regime do well and are more comfortable than those on strict bed rest, and it is believed that as good, if not better, results are secured

It is important that the physician know how much difficulty the patient has in moving his bowels and passing his urine while in bed Many patients can succeed only with much straining, especially in the use of the bedpan For these cases it is better to allow the use of a bedside commode, for this involves less physical strain than does a bedpan

After recovery the patient and physician should plan the future activities Usually, sedentary occupations may be undertaken in approximately 3 months Activities should be increased gradually, but vigorous exercises, fatigue, mental or emotional strain, and heavy occupation are denied The patient should be made to believe that he will be able to return to his former activities, including business, if they are made somewhat less strenuous than they were before the attack In general the measures recommended for Arteriosclerosis are applicable to these patients Every effort should be made to make the patient a useful, productive member of society The many restrictions frequently advised for the activities of these patients are undesirable and often cause them to become cardiac invalids

Peripheral Arterial Arteriosclerosis

Arteriosclerosis of the peripheral arteries often requires well-coordinated medical-surgical management, although it is a striking fact that a rigid palpable artery may function efficiently for years Of prime importance are the general measures to prevent complications These consist of daily skin care, foot hygiene, and the procedure to prevent infections as described under Diabetes Mellitus

Patients with demonstrably poor peripheral circulation should avoid trauma constricting clothing such as tightly laced shoes and garters, sitting with legs crossed, cramping postures, and extremes of heat or cold, they should wear warm clothing designed to protect the impaired limbs Infections and complicating diseases such as diabetes mellitus or gout should receive prompt and careful management Tobacco and vasospastic drugs, such as ergot compounds, must be discontinued If discontinuance of tobacco presents a serious problem (many question

causative allergens should be made and desensitization carried out if a definite allergy is found Cortocotropin in a dose of 40 to 100 mg daily or cortisone, 100 to 300 mg daily is of value in early cases Although the progress of the disease is ameliorated, complete cure is not secured Since the drugs are used over long periods of time they often cause serious reactions

Anemia should be relieved by blood transfusion Neuritis or pain from various sources may require meperidine (Demerol) hydrochloride, 100 mg by mouth 2 or 3 times a day Codeine phosphate, 30 to 60 mg 2 or 3 times a day is also helpful and may be employed instead of meperidine Occasionally morphine sulfate 8 to 15 mg subcutaneously 2 or 3 times a day, is required for relief of pain Since the disease is fatal the problem of addiction is not serious but morphine should be withheld as long as possible

Thromboangiitis Obliterans Buerger s Disease

The general measures described for Peripheral Arterial Arteriosclerosis should be instituted Emotional strain and tension are harmful and should be eliminated if possible Fatigue should be avoided and during periods when the disease is active increased rest is necessary Tobacco must be discontinued but small amounts of alcohol are beneficial

Pain may require acetylsalicylic acid 0 3 to 0 6 gm by mouth 3 or 4 times a day Codeine phosphate 30 to 60 mg , is effective also Codeine may be given in conjunction with acetylsalicylic acid if pain is severe Papaverine hydrochloride 30 mg by mouth 3 or 4 times a day, may help to relax spasm and increase circulation, with consequent relief of pain

Buerger's exercises are helpful and should follow this pattern Patient in recumbent position lifts legs to an inclined plane at a 45 angle and rests them on this plane for approximately 2 minutes until blanching occurs The legs then are dangled over the side of the bed and the feet and toes exercised for a few minutes until the pink color of increased blood supply is evident Legs are then elevated to bed level wrapped in warm woolen covers and rested on the bed for 5 minutes Cyanosis or pain may be avoided by shortening the period of dangling and the exercises of the feet The entire cycle may be repeated 5 times, permitting a 5 minute rest between cycles Three exercise periods a day

stasis, and papaverine hydrochloride in 30 mg doses intravenously or, better, intra-arterially if there is a palpable pulse proximal to the obstruction, given at 4-hour intervals for 24 to 48 hours, may relieve associated vascular spasm Dibenzyline, 40 to 80 mg in 4 divided doses, is also helpful in releasing vascular spasm Local heat any warmer than body temperature or extended for any period of time should be avoided The limb should be wrapped entirely in absorbent cotton If anti coagulant-papaverine or Dibenzyline therapy does not give a satisfac torily favorable response, the regional sympathetics should be blocked More and more, surgical removal of a diseased segment of an artery with end-to-end anastomosis or grafting of a piece of vein is being successfully carried out This operation is especially valuable in cases where an arteriosclerotic plaque is obstructing an otherwise functional artery

Visceral Arterial Arteriosclerosis

Arteriosclerosis of abdominal vessels is treated as described for arterio sclerosis in general Thrombosis of these arteries may call for prompt surgical intervention

Aortitis

Treatment is directed toward the underlying condition If syphilis or arteriosclerosis is causative, they should be treated Bed rest and avoidance of exertion or strain are wise until the underlying disease is under control Pain resembling that of angina pectoris is frequently observed, especially in syphilitic aortitis, and meperidine (Demerol) hydrochloride, 100 mg orally or intramuscularly, may be required for relief Occasionally temporary relief may be secured by nitroglycerin, 0 6 mg, dissolved under the tongue The longer-acting mannitol hexanitrate, 16 to 32 mg every 4 to 6 hours, may also prove helpful Aminophylline, 0 5 gm, given as a rectal suppository is occasionally beneficial

Periarteritis Nodosa

Treatment, except that for resultant symptoms, is unsatisfactory Supportive measures include a nutritious high vitamin diet, avoidance of fatigue and mental strain, and bed rest during acute episodes All medication should be discontinued A thorough investigation for

of any demonstrable etiology and not caused by nervous hyperactivity is known as essential hypertension depending upon its clinical course, this may be divided into benign and malignant varieties Hypertension also occurs secondarily as a complicating factor in a variety of diseases

Patients with hypertension must be evaluated carefully as a preliminary to proper management The degree of brain heart, and kidney impairment should be ascertained and used as a guide during treatment Since hypertension generally is a prolonged affair, any plan of treatment must be devised so as to take this into consideration

The value of making use of every available bit of psychic therapy cannot be stressed too vigorously The physician must continually reassure and instill confidence in his patient from the first thorough physical examination and the necessary supplemental studies down to the routine visits The chronic course of hypertension the meaning of, and factors influencing, blood pressure the effects of management, and the overall benign prognosis are all essential factors that should be discussed thoroughly with the patient The well informed and properly instructed individual can be a valuable assistant in the management of his own disease It is extremely important for the physician to have excellent rapport with, and the absolute confidence of his patient if maximum benefit is to be gained from psychotherapeutic measures

Rest is a useful therapeutic tool in the treatment of hypertension and, when properly employed can do much to relieve and control the disease Hypertensive patients should regulate their activities so that they secure 8 to 10 hours of sleep each night and a rest period of from 20 minutes to an hour in the middle of the day preferably after the noon meal Quiet week ends afford excellent opportunities for increased rest and can serve as catching-up periods Severe cases may require longer rest periods in order to avoid fatigue and to control symptoms

Fatigue is harmful and must be avoided Activities producing fatigue should be restricted or discontinued, but it is unwise to restrict activities to the extent of creating mental or physical tension Proper amounts of suitable physical exertion with its attendant physical and mental relaxation are definitely indicated and often prove to be of assistance in the management of the condition

Stress and strain on the vascular system whether produced by muscular exertion such as lifting heavy objects by coughing or sneezing or by straining at stool are unwise and patients must be instructed to avoid all such activities

are recommended As much can be accomplished by these simple exercises as is gained by the more expensive machines

Carefully regulated application of heat is soothing Immersion of the body in a tub of water warmed to 100° F is relaxing and stimulates circulation Great care must be taken to avoid burns and excess heat. Baths should be checked by the thermometer Heat pads, lamps, hot water bottles, and other non controllable sources of heat should be avoided

Elevation of body temperature by non-specific protein therapy often gives good results Typhoid vaccine is recommended start with an initial intravenous dose of 5 million organisms, increase this in subsequent injections by approximately 3 to 5 million, unless the temperature from the preceding dose exceeded 103° F or a chill occurred, in which case reduce the dose by a like amount Injections are to be given every 3 days unless the temperature has not fallen to normal after the preceding dose, in which case the next injection is delayed until the temperature is normal Usually 100 million organisms is the top level reached in this periodic increase in dosage Treatment may be continued for long periods of time provided improvement is apparent

Many drugs have been employed, but none has proved completely satisfactory Intravenous injection of a 5 per cent solution of sodium chloride 60 to 250 cc, depending on the age and general status of the patient, given once or twice a week, improves circulation Benzazoline (Priscoline) hydrochloride, 25 mg by mouth 5 or 6 times a day The doses of these drugs should be regulated carefully to the patient's needs and tolerance Corticotropin in a dose of 40 to 80 mg daily or cortisone, 100 mg daily, is helpful, but results are not permanent

In early cases sympathetic ganglionectomy is of definite value and, when performed by a surgeon skilled in its technique, is the most satisfactory therapy known at present When the disease has involved a portion of a larger artery, surgical removal of the diseased section with end to end anastomosis or vein graft may prove most helpful Crushing the perpheral nerve to desensitize a foot is also of value in patients who have painful ulcerating lesions of the toes Amputation is indicated when gangrene appears

Essential Hypertension

Abnormal elevation of the blood pressure occurring in the absence

2 or 3 cups of coffee or tea and one small cocktail should be taken in a day When nervousness is present it is wise to discontinue coffee and tea for a week or so to determine whether they are contributing factors

Various diets have been advocated in the treatment of hypertension The two that appear to be of the most value are the low sodium diet first advocated by Allen and more recently by Grollman, and the rice diet of Kempner, which incidentally is a low sodium diet also Neither of these is entirely satisfactory, and both are certainly without value in many patients Sufficiently good results have been obtained however, to warrant their trial, and in properly selected well managed cases especially those exhibiting early congestive failure excellent results may be secured Instructions must be rigidly adhered to if the maximum benefit is to be realized In the use of these diets group management including eating together has yielded the best results

Low sodium diet This diet limits the sodium intake to approximately 0 3 to 1 0 gm a day but permits a reasonable amount of protein It can be made fairly palatable through the proper selection of foods and the use of salt free milk Fluid intake is not to be limited The total daily calorie intake usually should be 1200 to 1800 calories All sources of sodium other than the diet must be avoided The sodium content of drinking water in most areas is usually 10 mg or less of sodium per 100 cc If it is higher than this distilled de ionized or bottled water with a low sodium content must be utilized Water treated in a water softener cannot be used Sodium chloride in cooking on the table, and in butter and bread must be eliminated No medicines that contain an appreciable amount of sodium are permitted since the sodium content of such drugs as sodium penicillin is only 4 mg per 100 000 units they may be used

Foods rich in salt must be avoided The following list gives some of the more common high salt containing foods

anchovies
bacon
baked beans canned
beef corned, dried roasted or canned
beef sausage
beef stew
beets and beet greens
bouillon cubes
Bovril
bread, unless salt free
butter unless salt free
canned fish meat, soup tomato juice vegetables
catsup
caviar
celery
celery salt
cheese
chili sauce
clams
crabs
curried meat
dates
duck
dumplings
fish paste
frankfurters
Grapenuts
haddock smoked
ham
kale
kidney
kipper
lobster

Emotional disturbances and factors creating mental stress are harmful, and measures must be taken by both the patient and the physician to avoid or limit their impact Hypertensive patients subjected to nervous tension, emotional turmoil, or fruitless competition and hopeless striving in their occupations should secure employment in which these harmful factors are absent or markedly reduced

Physical activities must be planned so as to afford the proper amount of exercise and relaxation without producing fatigue or undue stress and strain Exercises such as walking, fishing, bathing, automobile rides, horseback riding, gardening, and golfing usually are means of securing exercise, while at the same time there is mental relaxation without emotional tension Competitive games, whether they involve physical exertion or not, should usually be avoided Many highly nervous individuals show marked fluctuation in blood pressure when subjected to the exciting competition of card games or other games of chance Since hypertensive patients usually show the highest elevation of blood pressure in the evening, a definite effort must be made to avoid long fatiguing evenings Activities requiring tiresome mental or physical exertion and any situation that is likely to cause emotional disturbance should be discouraged

Education in the technique of relaxation for the tense, nervous, overactive patient is necessary It is often helpful to employ mild sedation until patients have learned to relax and are able to carry on their activities without unnecessary tension, but sedation can be, and often is, overdone in the treatment of hypertension Occasionally patients have emotional tensions of such degree as to require psychiatric assistance before any satisfactory degree of relaxation can be secured

The diet in hypertension is important from several aspects It is absolutely essential to successful treatment that patients not be overweight, if they are overweight, they must be reduced to normal weight or slightly below A gradual loss of weight of not more than 1 or 2 pounds a week is satisfactory A reducing schedule as outlined for obese patients is satisfactory Restriction of fat, cholesterol, and protein intake to moderate amounts is recommended, but not at the expense of making the diet unappetizing Coffee tea, and modest amounts of alcohol are permissible if they do not lead to undue stimulation Nervousness, insomnia, and restlessness may be brought about or aggravated by one of these beverages, if this is true, it should be omitted Excessive intake of any of these must be interdicted As a general rule, no more than

Miscellaneous

Beverages	ale	juices—fruit or vegetable fresh or canned when containing no sodium
	coca-cola	tea
	cocoa—made with salt poor milk (Lonalac)	
	coffee	

Condiments Desserts Flavorings

allspice	jam	pepper
cinnamon	jelly	sugar
fruits	lemon extract	tapioca
gelatin plain	paprika	vanilla extract
honey		vinegar

Cooking fats

lard unsalted	Spry	Crisco

Salt poor bread can be purchased in most cities or can be prepared easily in the home if necessary A palatable salt poor bread can be made by using salt free milk (Lonalac) as manufactured by Mead Johnson Company The recipe for a pound loaf is

flour – 2½ cupfuls
sugar – 1½ tblsp
Spry – 1 level tblsp
Lonalac – 3 level tblsp
lukewarm water – 7 ounces
yeast – ½ cake

The ingredients and the bread are prepared in the usual manner A less palatable salt poor bread may be made without milk by following this recipe

flour – 4 cupfuls
sugar – 3 tblsp
Spry – ½ cup
water – 4 cupfuls
yeast – 2 ounces
Follow usual bread making procedure

Typical salt poor menus prepared from the lists above are as follows

macaroni and cheese
malted milk
mayonnaise
meat paste
meat juices and soups
milk condensed
molasses
mustard
nuts salted
oleomargarine
olives green and stuffed
Ovaltine
Oxo
pastries
peas green canned
popcorn salted
pork sausage
Post Toasties
potatoes chip soups
pretzels
relishes
Ry Krisp
salmon canned
sardines canned
sauerkraut
sausage
seafoods (most of them)
smoked foods
sauces (most of them)
shrimp
tongue ox pickled
Zwieback

A properly balanced diet may be obtained by seeing that the following essential foods are eaten each day

bread salt free
butter salt free
cereals at least ½ cupful
vegetables 3 or 4 servings
fruit 2 or 3 servings
meat fish or fowl 2 to 4 ounces
milk use salt free milk powder (Lonalac Mead Johnson Company) add 2½ cupfuls of water to ⅔ cupful of powder

These may be chosen from the following list of low salt containing foods

Cereals

barley pearled
bran wheat
corn meal
Farina plain
Instant Ralston
oatmeal
Puffed Rice
Puffed Wheat
rice
Shredded Wheat
Wheatena
wheat germ

Fruit All fresh fruit and all canned dried or frozen fruits that are not preserved with sodium-containing compounds such as sodium benzoate or to which salt has not been added

Meats fresh or frozen avoid canned dried or smoked

beef
chicken breast meat
fish except shellfish
lamb
liver
mutton
pork
rabbit
turkey
veal

Vegetables

asparagus
beans, green
beans kidney lima, navy
broccoli
brussels sprouts
cabbage
carrots
cauliflower
corn
cowpeas
eggplant
hominy
leeks
lettuce
mushrooms
okra
onions
parsnips[1]
peas[1] fresh or frozen
peppers
potatoes
pumpkin
rice
squash
tomatoes
turnip

of fat It contains less than 0 1 gm of sodium daily The total calories may be reduced to 1500 daily or less if weight reduction is desired The diet is prepared in the following manner

Each day one cupful of uncooked rice (white, brown or polished) is measured out and divided into portions according to the desires of the patient It is cooked by boiling or steaming No salt, milk, fat or seasoning of any kind is added either before or after cooking, but the hot servings may be flavored with fruit juice, dextrose, pure jam or jelly, honey, or white sugar Maple sugar, corn syrup and molasses are to be avoided Fresh raw, or cooked fruits except avocado pears dates, nuts bananas, and tomatoes are permitted Frozen fruits may be used when desired Fruit juices fresh or canned except tomato or vegetable juices and those prepared with artificial flavoring or sodium containing preservatives may be used Total fluids are limited to 3 or 4 cups of fruit juice a day for a few days after the diet is started

One or 2 tablets or capsules of a suitable multivitamin preparation (Multicebrin Unicaps) given each day are recommended to insure adequate vitamin intake Patients who become excessively hungry between meals and are not overweight may munch on rice brittle candy No other food or drink of any kind is permissible for a least 6 weeks to 2 months At that time small amounts of potatoes and meat may be added If the blood pressure remains down the meat and vegetables may be increased until about one third of the fruit is replaced by vegetables The diet is then adjusted according to the patient s needs

Patients on the rice diet must be followed closely by the physician and continually encouraged to maintain the regimen Occasional checks of urinary chloride excretion are helpful in determining whether the patient is adhering to his diet The usual urinary chloride excretion of patients on an average diet varies between 100 to 200 milliequivalents per liter in 24 hours whereas that of patients on the rice diet is 10 milli equivalents per liter or less This diet is monotonous often unpalatable, and seems a starvation diet to many patients consequently failures are frequent Better results are often obtained if the patient is kept in the *hospital during the early weeks of this routine Such periods help him become accustomed to the rigid nature of the diet and get him past the* most crucial period of adjustment Starting several patients on the diet together and thus utilizing group therapy, is helpful To this might be added the club atmosphere of eating together in a pleasant place

Drugs In the past five years numerous drugs have been introduced for

Breakfast

orange juice ½ cup
oatmeal ½ cup
egg 1 boiled
butter 1 pat
bread 1 slice
coffee 1 cup
sugar 1 teasp
cream, 1 teasp

or

grapefruit ½ medium
Farina ½ cup
egg 1 poached
butter 1 pat
bread 1 slice
coffee 1 cup
milk (Lonalac) 1 glass

Luncheon

lamb 2 ounces
potato 1 medium
squash 1 serving
lettuce 1 leaf with
  cut apples
baked apple 1 medium
butter 1 pat
bread 1 slice
coffee 1 cup with sugar
  and cream *or*
milk (Lonalac) 1 glass

or

turkey small serving
brussels sprouts 1 serving
turnip 1 serving
lettuce 1 leaf with
  chopped apple
grapefruit ½ medium
butter 1 pat
bread 1 slice
coffee 1 cup with cream
  and sugar *or*
tea

Supper

chicken small serving
rice ½ cup
onion 1 small
lettuce 1 leaf with ½ pear
banana 1 sliced
butter 1 pat
bread 1 slice
coffee 1 cup with sugar
  and cream *or*
milk (Lonalac) 1 glass

or

swordfish small serving
  broiled with lemon
asparagus fresh 6 stalks
peas fresh 1 serving
lettuce 1 leaf
tomato ½ small
peach small
butter 1 pat
bread 1 slice
coffee 1 cup with cream
  and sugar

Patients on low-sodium diets must be checked carefully at frequent intervals in order to detect any signs of sodium deficiency During hot weather, diarrhea, fever, or vomiting, care must be taken to avoid sodium imbalance At the first signs of weakness, muscle cramps, or malaise more sodium must be added to the diet until symptoms disappear Usually this can be accomplished by adding salted bread and butter to the diet, if serious symptoms are not present The diet may be planned to bring about gradual weight loss or may be prepared with low cholesterol content, if so desired Patient's tastes, habits, likes, and dislikes must be considered in preparing the diet, if good results are to be secured The more palatable the diet and the more nearly it approximates the usual diet for the patient, the greater are the chances of securing successful dietary treatment Patients should remain on low-sodium diets indefinitely unless hypertension disappears Then a diet with moderate sodium content may be tried

Rice Diet The rice diet advocated by Kempner consists of 200 to 300 gm of rice (approximately 1000 calories) and sufficient fruit fruit juice, and sugar to make up a total of 2000 calories This diet furnishes approximately 20 gm of protein 450 gm of carbohydrate, and 5 gm

This may lead to gastric irritation and initiate or reactivate a peptic ulcer It leads to large bowel irritation and cramps and diarrhea may be produced in susceptible patients Care, therefore, should be employed in using it in the presence of an irritable colon, ulcerative or mucous colitis

A pure alkaloid of Rauwolfia serpentina, reserpine marketed under the trade names of Sandril, Serpasil with actions similar to those of the crude root, is also widely used In the treatment of hypertension it may be given as a single dose 0 1 to 0 25 mg after breakfast or at bedtime Some prefer doses of 0 25 mg 2, 3 or 4 times a day Long continued use especially with higher doses, however, may cause the mental depression and other untoward effects seen with the crude drug An interesting complication, when large doses of the purified alkaloid are used, is the development in some patients of the characteristic findings of paralysis agitans This must be watched for and the drug stopped promptly if it occurs

Ganglionic Blocking Compounds These agents act by blocking sympathetic and parasympathetic nerve ganglia, thereby decreasing peripheral resistance and lowering blood pressure The lowered blood pressure tends to be greatest in the standing position, less marked in the recumbent position Their dosages should be so regulated that the trough of systolic pressure in the standing position is no lower than 120 mm mercury If they should cause faintness or dizziness during the day, the patient usually needs only to lie or sit down They also produce constipation, blurring of vision, dryness of the mouth and in the male loss of ejaculation

The first of these compounds to be widely used was hexamethonium (*Methium*) *chloride Erratic absorption by mouth causes the dosage to* vary widely tolerance to the drug often develops and as a result, frequent reactions occur making its use alone by mouth not very satisfactory The best results with hexamethonium chloride are obtained by subcutaneous injection The parenteral dose intravenous or subcutaneous should be started with 5 or 10 mg given at 6 to 12 hour intervals and increased according to the response of the patient The intravenous route may be used in active hypertensive emergencies With the patient seated give 0 5 to 1 0 mg slowly with continual observation of the blood pressure in the other arm Patients with increased intracranial pressure severe arteriosclerosis and azotemia are especially sensitive to the intravenous administration of the drug and if excessive fall in blood pressure occurs the patient should be placed in the Trendelenberg position and

Breakfast	*Luncheon*	*Supper*
orange juice ½ cup	lamb 2 ounces	chicken small serving
oatmeal ½ cup	potato 1 medium	rice ½ cup
egg 1 boiled	squash 1 serving	onion 1 small
butter 1 pat	lettuce 1 leaf with cut apples	lettuce 1 leaf with ½ pear
bread 1 slice	baked apple 1 medium	banana 1 sliced
coffee 1 cup	butter 1 pat	butter 1 pat
sugar 1 teasp	bread 1 slice	bread 1 slice
cream, 1 teasp	coffee 1 cup with sugar and cream *or*	coffee 1 cup with sugar and cream *or*
	milk (Lonalac) 1 glass	milk (Lonalac) 1 glass
or	*or*	*or*
grapefruit, ½ medium	turkey small serving	swordfish small serving broiled with lemon
Farina, ½ cup	brussels sprouts 1 serving	asparagus fresh 6 stalks
egg 1 poached	turnip 1 serving	peas fresh 1 serving
butter 1 pat	lettuce 1 leaf with chopped apple	lettuce 1 leaf
bread 1 slice	grapefruit ½ medium	tomato ½ small
coffee 1 cup	butter 1 pat	peach small
milk (Lonalac) 1 glass	bread 1 slice	butter 1 pat
	coffee 1 cup with cream and sugar *or*	bread 1 slice
	tea	coffee 1 cup with cream and sugar

Patients on low-sodium diets must be checked carefully at frequent intervals in order to detect any signs of sodium deficiency During hot weather, diarrhea, fever, or vomiting, care must be taken to avoid sodium imbalance At the first signs of weakness, muscle cramps, or malaise more sodium must be added to the diet until symptoms disappear Usually this can be accomplished by adding salted bread and butter to the diet, if serious symptoms are not present The diet may be planned to bring about gradual weight loss or may be prepared with low cholesterol content, if so desired Patient's tastes, habits, likes, and dislikes must be considered in preparing the diet, if good results are to be secured The more palatable the diet and the more nearly it approximates the usual diet for the patient the greater are the chances of securing successful dietary treatment Patients should remain on low sodium diets indefinitely unless hypertension disappears Then a diet with moderate sodium content may be tried

Rice Diet The rice diet advocated by Kempner consists of 200 to 300 gm of rice (approximately 1000 calories) and sufficient fruit, fruit juice, and sugar to make up a total of 2000 calories This diet furnishes approximately 20 gm of protein, 450 gm of carbohydrate, and 5 gm

5 to 10 mg, and then gradually increased as the patient adjusts Since serious hypotension frequently occurs after the first dose, it should be given while the patient is in the hospital or under very careful observation This drug retains the untoward effects of the other members of the group and unfortunately causes considerable blurring of vision The visual disturbance is so serious in many patients that it forces discontinuance of the drug, the continual use of pilocarpine nitrate, or preparation of specially ground glasses

Certainly the most desirable ganglionic blocker has not yet been obtained but there is hope that one will be discovered which will have long action preferably 12 to 24 hours and be relatively free from undesirable effects

Another group of drugs recently heralded in the treatment of hypertension are the *hydralazines* Of these the most effective and widely used is 1 hydrazinophthalazine (Apresoline) or hydralazine hydrochloride It is a central adrenergic blocking agent with direct vasodilator properties which lowers systolic and diastolic pressures and at the same time, increases cardiac output and blood flow through the kidneys It causes tachycardia and in occasional cases produces angina pectoris which may preclude its use Hydralazine has been found helpful in severe, especially malignant, hypertension and in hypertension which persists or recurs after sympathectomy With advanced renal disease however the drug does not prevent further deterioration of the kidneys

The initial oral dose should be 25 mg after each meal and at bedtime which may be increased the second week to 50 mg four times a day if such untoward effects as headache palpitation or postural hypotension do not interfere The usual maximum dose is 100 mg 4 times a day Parenteral hydralazine should be used only in comatose patients, or where the drug cannot be administered orally Usually a dose of 20 to 30 mg intravenously or intramuscularly is satisfactory If there is marked renal damage a smaller dosage is indicated

Other undesirable effects may include dizziness numbness and tingling of extremities localized edema malaise anxiety and even disorientation and depression In some patients an influenza like syndrome may occur during the first week of therapy A most interesting complication has been the development in some patients particularly those on 400 mg or more a day for 8 months or longer of an arthritic syndrome This resembles rheumatoid arthritis or lupus erythematosus with sometimes

the treatment of hypertension, some of which have proved to be quite satisfactory, at least in reducing the level of systolic and diastolic pressure, but all of which, when effective, manifest certain side effects. Rather extensive clinical trials with those to be discussed here have demonstrated at least two principles in their effective use (1) patients seem to do better over a long period of time when careful selection of drugs is made, with changes from time to time from one drug to another, and (2) combinations of drugs often are more effective than any one drug used singly Combination therapy applies also to the use of drugs following sympathectomy for hypertension

Sedation with phenobarbital, 15 mg by mouth 4 times daily is definitely useful in the tense, overactive patient who is unable to relax It serves as a useful tool in helping the patient learn habits of relaxation but great care must be taken to prevent overuse of sedatives and to keep the patient from becoming habituated to them, as often happens Sedatives should be omitted periodically for several days to determine whether they have been beneficial Not infrequently it will be found that the patient gets on better without a sedative

When phenobarbital is unsatisfactory and a mild more effective agent is needed, Rauwolfia serpentina, and its derivatives should be given It is effective, particularly in early hypertension and with neurogenic hyperactivity, and sometimes surprisingly so in some cases of chronic hypertension The exact mode of action of Rauwolfia is not known but it is thought to effect chiefly the pressure-regulating centers in the hypothalamus It tends to be slow in its action requiring from 7 to 14 days to give full effect which, however, may persist for 10 to 14 days after cessation of the drug Often it can be used for long periods with minimum side-effects

The crude whole extract of Rauwolfia (Raudixin) is given in an initial dose of 50 mg 3 or 4 times a day and gradually increased to 300 or 400 mg daily It exerts a relaxing and quieting effect on the nervous system Bradycardia is commonly observed Frequently, Rauwolfia gives rise to nasal congestion, which may be severe, produces epistaxis, leads to sinusitis, or causes so much discomfort as to preclude the use of the drug Some relief may be obtained by the use of antihistamine drugs with long action such as pyrrobutamine (Co-Pyronil) 1 pulvule every 6 to 12 hours Rauwolfia also may cause lethargy and mental depression which in some patients is severe When such occurs the drug should be discontinued It also increases gastric secretion including hydrochloric acid

paragangliomas, while phenoxybenzamine, tolazoline, and azepetine are employed for the therapy of peripheral vascular disorders

Combined Drugs With numerous drugs available which have differing modes of action it is reasonable that combinations of these drugs should be tried We shall not attempt to describe all possible combinations but rather to mention a few that have proved helpful when used carefully We do not advocate combined drugs in one pill, rather each preparation should be tailored to the individual s requirements

For early and mild hypertension not responding well to diet, rest and phenobarbital or reserpine, a combination of reserpine, 0 1 to 0 25 mg, given after breakfast plus phenobarbital 15 mg after meals and at bed time is useful It should be cautioned that in some patients the sedative effect may be too much

Patients with somewhat more severe hypertension who are not doing well on a combination of reserpine and phenobarbital may benefit from a combination of rauwolfia, 12 5 or 25 mg phenoxybenzamine, 2 5 or 5 mg, and protoveratrine 0 1 or 0 2 mg (Miopressin No 1 and No 2) A starting dose of Miopressin No 1 if the case is very mild or Miopressin No 2 1 capsule every 8 hours increased to 1 capsule every 4 hours in 3 or 4 days if necessary, may be tried Occasionally, patients will require *8 to 12 capsules daily for adequate effect Usually there is little* in the way of untoward effects the nose, of course, is stuffy and some mild orthostatic hypotension occurs if the dose is too much Appetite, bowels bladder vision and all other functions except ejaculation are usually well preserved Ejaculation is impaired as with any of the adrenergic or ganglionic blockers The dose is rather easily regulated This preparation however is too weak to be of use for other than the mild to moderately severe hypertension patients

A newer, and more effective combination for early and mild to moderate hypertension is Rauwolfia or its alkaloid and pentolinium tartrate The Rauwolfia crude root is to be given 25 or 50 mg 3 or 4 times a day or the alkaloid reserpine 0 25 mg 3 or 4 times a day, with pentolinium tartrate (Ansolysen) 20 mg morning and night In protracted cases the latter may be increased to 20 mg 3 or 4 times a day and if this is not sufficient the dose may be increased to 30 mg 40 mg 50 mg, or more 3 or 4 times a day until pressures come under control

A combination that has received extensive trial especially in severe and particularly malignant hypertension is hexamethonium with hydrazinophthalazine In the literature this has come to be known as the

if necessary, vasoconstrictors, such as phenylephrine (Neo synephrine) hydrochloride, 2 to 4 mg, or norepinephrine (Levophed) 2 to 4 mcg, be given slowly intravenously

If the oral route is desired, hexamethonium chloride may be given in an initial dose of 125 mg 3 or 4 times a day and gradually increased Usually 3 0 gm daily should not be exceeded for most patients Occasionally higher doses are tolerated When the oral route is used constipation must be particularly guarded against Constipation should be treated as recommended on page 528

In occasional cases hexamethonium has been found to cause the sudden onset of a strange and rapidly fatal form of acute interstitial fibrosis of the lungs Its nature is unknown and no remedy has been found for it.

One of the newer ganglionic blockers, and the one used widely at present, is pentolinium tartrate (Ansolysin) It can be administered orally to give smooth control over blood pressure levels and is most useful in severe hypertension By weight it is said to be 5 times as effective in lowering elevated blood pressure as hexamethonium chloride, ion for ion it is 10 times as powerful The starting dose is 20 mg 2 and then 3 times a day Smirk has emphasized that to secure uniform absorption, the tablet should be given one-half hour before meals The dosage should be increased gradually to 40 mg, 60 mg etc up to as much as 200 mg 2 or 3 times a day, with strict accuracy of dosage maintained As with the others of these compounds, pentolinium tartrate causes constipation It is recommended that with this drug 15 to 30 mg of neostigmine be given orally upon arising, and if constipation persists, a saline laxative should be given at bedtime In moderate to severe hypertension Rauwolfia alkaloid, such as reserpine, can be combined very effectively with pentolinium, with further reduction in blood pressure and with smaller doses of pentolinium tartrate (See combined therapy)

The most recently introduced ganglionic blockers are mecamylamine (Inversine) hydrochloride and chlorisondamine (Ecolid) Experience with both is, as yet, very limited but each has already demonstrated individual merit Mecamylamine in doses of 5 to 20 mg 2 to 4 times a day seems to exert a smoother hypotensive effect which lasts an hour or so longer than the hexamethonium effect Although the untoward effects are similar to those of other ganglionic blockers they are possibly somewhat milder Chlorisondamine in a dose of 25 to 200 mg orally morning and evening is undoubtedly the longest acting ganglion blocker at present available This is its chief merit The initial dose should be small,

paragangliomas, while phenoxybenzamine tolazoline and azepetine are employed for the therapy of peripheral vascular disorders

Combined Drugs With numerous drugs available, which have differing modes of action it is reasonable that combinations of these drugs should be tried We shall not attempt to describe all possible combinations but rather to mention a few that have proved helpful when used carefully We do not advocate combined drugs in one pill rather each preparation should be tailored to the individual's requirements

For early and mild hypertension not responding well to diet rest and phenobarbital or reserpine a combination of reserpine 0 1 to 0 25 mg, given after breakfast plus phenobarbital, 15 mg, after meals and at bedtime is useful It should be cautioned that in some patients the sedative effect may be too much

Patients with somewhat more severe hypertension who are not doing well on a combination of reserpine and phenobarbital may benefit from a combination of rauwolfia 12 5 or 25 mg, phenoxybenzamine 2 5 or 5 mg, and protoveratrine, 0 1 or 0 2 mg (Miopressin No 1 and No) A starting dose of Miopressin No 1 if the case is very mild or Miopressin No , 1 capsule every 8 hours increased to 1 capsule every 4 hours in 3 or 4 days if necessary, may be tried Occasionally, patients will require 8 to 12 capsules daily for adequate effect Usually there is little in the way of untoward effects, the nose of course is stuffy and some mild orthostatic hypotension occurs if the dose is too much Appetite bowels, bladder, vision, and all other functions except ejaculation are usually well preserved Ejaculation is impaired as with any of the adrenergic or ganglionic blockers The dose is rather easily regulated This preparation, however is too weak to be of use for other than the mild to moderately severe hypertension patients

A newer and more effective combination for early and mild to moderate hypertension is Rauwolfia or its alkaloid and pentolinium tartrate The Rauwolfia crude root is to be given 25 or 50 mg 3 or 4 times a day or the alkaloid reserpine 0 25 mg 3 or 4 times a day, with pentolinium tartrate (Ansolysen) 20 mg morning and night In protracted cases the latter may be increased to 20 mg 3 or 4 times a day and if this is not sufficient the dose may be increased to 30 mg, 40 mg, 50 mg or more 3 or 4 times a day until pressures come under control

A combination that has received extensive trial especially in severe and particularly malignant hypertension is hexamethonium with hydrazinophthalazine In the literature this has come to be known as the

the occurence of lupus erythematosus (L E) cells in the peripheral blood and occasional hepatic damage as shown by abnormal cephalin cholesterol flocculation tests

Veratrum Derivatives Another recent drug, with central nervous system action which gives peripheral vasodilation is protoveratrine, a mixture of two purified alkaloids derived from Veratrum album It is useful particularly in the management of hypertensive headaches Occasionally, it may produce a substernal burning sensation that is not to be confused with angina pectoris It does not have the postural hypotensive effects of the ganglionic blocking agents It increases vagal tone which causes bradycardia, and sometimes partial, or even complete, A-V dissociation These effects can be prevented by atropine Since this cardiac slowing effect is similar to that of digitalis, the use of protoveratrine may cause some confusion if it is given during intensive digitalization It is also a rather powerful emetic and there is no good antidote for it

Protoveratrine is best administered in an initial dose of 0 5 to 0 75 mg orally with breakfast, followed in 2 hours by a small booster dose of 0 25 mg The same schedule may be used with dinner, followed by a booster dose of 0 25 mg 2 hours later It is best to give the drug in this dosage no more than once or twice daily at intervals of at least 8 hours It should not be administered less than 2 hours preceding a meal

Protoveratrine may be given intravenously and in acute situations, 1 2 to 1 9 micograms per kilo body weight intravenously, in a single injection usually is effective The dose may be repeated every 3 to 4 hours Intravenous administration by constant drip may be used but this requires the utmost vigilance Maximum effects lag 10 to 15 minutes behind injection, therefore, severe nausea, or cardiac arrhythmia may occur suddenly and require atropine, 0 5 to 0 6 mg or more, for relief

Other hypotensive medication may be used in conjunction with protoveratrine to make more smooth the levels of blood pressure in the remaining 24 hours of the day

Adrenolytic and Vasodilator Agents These agents lower blood pressure but are too transient or erratic in their effects, and sometimes too toxic, for long-term administration in the treatment of hypertension. They include such substances as phenoxybenzamine (Dibenzyline) hydrochloride, phentolamine (Regitine) hydrochloride, piperoxan (Benodaine) hydrochloride, tolazoline (Priscoline) hydrochloride, azepetine (Ilidar), and similar preparations Phentolamine and piperoxan are used primarily for the diagnosis and treatment of pheochromocytomas or

4th day—500 mg hexamethonium chloride every four hours Omit part or all of dose, depending upon level of systolic pressure, as described below

5th day—Same plus 25 mg 1 hydrazinophthalazine every 4 hours

6th day—Same plus 50 mg 1 hydrazinophthalazine every 4 hours

7th day—Same plus 75 mg 1 hydrazinophthalazine every 4 hours

8th day—Same plus 100 mg 1 hydrazinophthalazine every 4 hours

The establishment of normotension would interrupt and stabilize the above schedule at any point.

Routine orders are as follows (1) measure blood pressure before each dose (every four hours) and record on graphic chart (2) Give—mg (full dose) of hexamethonium chloride if systolic pressure is 140 mm Hg or above (3) Give—mg (½ dose) of hexamethonium chloride if systolic pressure is between 130 and 140 mm Hg (4) Give—mg (¼ dose) of hexamethonium chloride if systolic pressure is between 120 and 130 mm Hg (5) Omit all hexamethonium chloride if systolic pressure is below 120 mm Hg (6) *Do not omit* hydrazinophthalazine (7) Give cascara and milk of magnesia or other mild laxative every evening if no bowel movement occured that day Do not allow patient to become constipated Do not use bulky' laxative or roughage ' Use irritative and saline laxatives Citrate of magnesia is given in the morning if the evening laxative is not effective It is essential that the patient have a bowel movement every day (8) Give urecholine 5 to 10 mg by mouth for distention severe constipation and retention of urine in the bladder Do not give urecholine parenterally as severe reactions may occur the parasympathetic nervous system is probably sensitized to peripherally acting cholinergic drugs

In the most severe (malignant) cases the dose of hexamethonium chloride may be increased to 1 0 gm every 4 hours and the dose of 1 hydrazinophthalazine to 200 mg every 4 hours 750 mg and 150 mg respectively per dose, according to Schroeder, will be adequate to control over 90 per cent of cases At these levels severe constipation may be intolerable unless bowels are kept open daily

As this is a very vigorous and intensive form of therapy, certain side effects must be watched for Orthostatic hypotension is common if the blood pressure is lowered too rapidly or too far If the patient has had previous sympathectomy for hypertension the hyphex treatment usually will cause an excessive postural fall in blood pressure requiring modification of the treatment Hexamethonium chloride is the drug

Hyphex treatment. Such a combination utilizes a ganglionic blocking agent with a centrally acting drug and a peripheral vasodilator Schroeder, who has developed this combination, has felt satisfied from his studies that neither drug alone will reduce adequately or control severe hypertension as will the proper use of the two drugs together At the same time he is quick to point out that these two agents, used together, are not without hazard, particularly in Negroes, and in the presence of uremia and cerebral arteriosclerosis Their use, however, appears to be justifiable when severe damage secondary to hypertension has occured and the situation is desperate

Except in patients who have previously had a sympathectomy for hypertension, to be mentioned later, strict adherence to a schedule must be maintained if the best results are to be achieved with a minimum of undesirable side effects The following is taken from Schroeder's recommendations

The patient must be in a hospital Blood pressure is measured in the supine position, every 4 hours, day and night Renal function is estimated by the 15, 30, and 60 minute excretion of intravenously excreted phenol red (P S P) The non-protein nitrogen level of the blood is determined Renal status is evaluated by intravenous pyelography and careful urinalysis The heart is examined by electrocardiography and X ray and the status of the blood vessels by funduscopic examination

Schroeder s recommendation of drug therapy is as follows

Hexamethonium chloride is given by mouth and increased to effective levels at a rate depending upon the severity of the hypertension, its lability, and the amount of vascular damage, especially cerebral Every effort is made to undershoot' the dose, and to build up toward the desired effect Dosage schedule is changed daily, slowly and carefully, depending upon the record of the previous day

1-Hydrazinophthalazine (Apresoline) is added later A typical schedule for a case of severe arterial hypertension without renal insufficiency or marked cerebral arteriosclerosis follows

1st day—125 mg hexamethonium chloride every 4 hours Omit dose if systolic pressure is below 140 mm Hg

2nd day—250 mg hexamethonium chloride every four hours
3rd day—375 mg hexamethonium chloride every four hours

hypertension similar to the use of the (Hyphex) treatment discussed in preceding paragraphs This newer combination is not as well established as the (Hyphex) program but one may begin with pentolinium tartrate (Ansolysin) 20 mg 3 times a day and 1 hydrazinophthalazine (Apresoline) 25 mg 3 times a day, and depending upon the urgency of the situation, increase both drugs rather rapidly to an average dose of 100 mg four times a day

Potassium thiocyanate is of limited value and as a primary form of treatment for hypertension is being used less and less Occasionally it is useful, however in the treatment of hypertensive headaches as discussed in a later paragraph on headache For the treatment of hyper tension, a dose of 0 2 gm 3 times a day by mouth either as the elixir or as enteric coated tablets is recommended The maintenance dose may vary from 2 to 1 0 gm daily The blood level of the drug must be followed carefully An initial blood level of 8 to 12 mg per cent is desirable this is then reduced and maintained at 4 to 6 mg per cent, if a favorable reduction in blood pressure is secured Used alone in the treatment of hypertension it fails more often than not. Potassium thiocyanate must not be administered to patients with renal damage arteriosclerosis, blood dyscracias, such as thrombocytopenic purpura drug hypersensitivities osteoporosis (with poor bone healing) or severe con gestive heart failure or to those unable to have the drug levels of the blood checked The many toxic reactions and the lack of favorable response in many cases have been sufficient to cause extensive abandonment of this drug

The nitrites and the xanthines such as theobromine and mannitol hexanitrate, are of little or no value in the treatment of hypertension The action of the nitrites is transient Larger doses of the longer acting nitrites produce severe headaches and other symptoms of toxicity

Unfortunately the use of hypertensive drugs does not remove the exciting cause of the hypertension and consequently gives only sympto matic relief Frequently the undesirable side effects such as headache, dizziness, dyspnea, giddiness constipation, and the collapse which oc casionally follows prevent their use A continuing search for new drugs and careful critical, evaluation of them should in time lead to a much more satisfactory treatment of hypertension

Digitalization is recommended if there is any evidence of cardiac insufficiency Occasionally patients with severe hypertension who ap parently do not have any demonstrable congestive failure show excellent

reduce under such circumstances, rather than the 1-hydrazinophthalazine A generalized lymph-adenopathy, splenomegaly, and hyperglobulinemia may occur with treatment Presumably these are of no serious significance Occasionally microscopic hematuria develops The hydrazinophthalazine may cause chest symptoms indistinguishable from angina pectoris, or it may give rise to a febrile reaction with joint symptoms, like rheumatoid arthritis or lupus erythematosus This febrile arthritis picture occurs in about 7 per cent of patients on hyphex treatment. Impotence is common in males and prostatic obstruction occurs rather frequently Hexamethonium chloride may cause a curious acute interstitial fibrosis of the lungs which may prove to be rapidly fatal At present there is no known treatment for this condition once it develops It has been seen mostly in Negroes, in cases of malignant hypertension Dosage may be a factor

Numerous other combinations of these newer antihypertensive drugs are receiving trial, but their optimum dosage in combination, and the cases in which they produce the best results, will require further observation Several of these combinations will be described

(1) *Reserpine and 1-hydrazinophthalazine (Apresoline)* The dose of reserpine should be reduced to 0 25 mg twice a day, and 25 mg of hydrazinophthalazine given 4 times a day for 2 weeks If results are not satisfactory, continue the dose of reserpine the same, but increase the 1 hydrazinophthalazine over 10 to 14 days to 200 mg a day

(2) *Rauwolfia with hydrazinophthalazine* Use 50 to 100 mg of Rauwolfia 3 times a day, and if not sufficient, add hydrazinophthalazine (Apresoline) 10 mg by mouth at meals and at bedtime, increasing the dosage gradually, if necessary to 25 mg or even 50 mg 4 times a day The patient should be warned to reduce (not discontinue) the dosage if the symptoms of headache and/or palpitation are distressing but to resume a gradually increasing dosage as rapidly as possible

(3) *Mecamylamine (Inversine) with hydralazine* The combination of mecamylamine with hydralazine or reserpine is currently giving most satisfactory results and is the present choice of the authors Mecamylamine is given orally initially in a 5 mg dose every 6 hrs and each dose increased 2 5 or 5 0 mg on the next day Hydralazine is added on the 5 day in the same dose and schedule as recommended for hexamethonium treatment

(4) *Pentolinium tartrate (Ansolysin) with 1 hydrazinophthlazine (Apresoline)* This combination should be used only in cases of severe

seems to have been of definite value The operation should be extensive —such as the lumbothoracic sympathectomy of Smithwick—to obtain maximum benefit Patients must be selected carefully if good results are to be obtained Ideally these patients should be those under 50 years of age who have failed to respond to medical management, possess good renal function have little or no arteriosclerosis, and show favorable response to cold pressor and sedation tests Renal function must show no retention of nitrogen and the phenolsulfonphthalein test must show at least 15 per cent, preferably 25 per cent, excretion in 15 minutes Operation should not be performed until congestive failure is relieved and compensation restored At least 6 months should elapse following myocardial infarction and 6 weeks to 3 months following a cerebral vascular accident After sympathectomy patients must be instructed about the danger of sudden hypotension and taught to wear elastic bandages on the legs and properly fitted abdominal binders with elastic pressure pads Operation usually relieves headache and, in a properly selected group, prolongs life Approximately 10 per cent of the cases secure cures of their hypertension After operation, medical treatment of hypertension should continue

Unilateral nephrectomy in an extremely small percentage of hypertensive patients with unilateral renal lesion must be considered The hypertension of these patients may be a result of disease in one kidney In general, results have not been good, and the decision for nephrectomy should rest on the need for surgical removal of the diseased kidney rather than on any hope that an associated hypertension will be relieved Occasionally, however, highly favorable results do follow the removal of a diseased kidney

Paroxysmal Hypertension

This form of hypertension is usually caused by a pheochromocytoma paraganglioma, or *chromaffin cell tumor* of the adrenal gland *Treatment* should consist of the surgical removal of the tumor If the tumor has been causative of the hypertension results are excellent after all of the tumor has been excised

Postural Hypertension

In this rare condition blood pressure becomes elevated when the patient assumes the erect position The disease is thought to result

response to adequate digitalization Dyspnea is relieved, fatigue is not so severe, strength increases, and the blood pressure may fall These patients actually have mild cardiac insufficiency but not overt congestive failure The fact that digitalis influences the kidney to excrete sodium may also be a factor in this beneficial effect

Mercurial diuretics also give excellent results if there is edema, and frequently they are helpful also in the borderline cases where there may be no clinical evidence of edema These drugs, like digitalis, help to bring about decreased dyspnea and a fall in blood pressure as compensation is gained They should be given as outlined for Congestive Failure

Female hypertensive patients in the menopause who are tense, nervous, and emotionally unstable are benefited by adequate sex hormone therapy Not infrequently relief from the distressing menopausal symptoms exerts a favorable influence on the hypertension Diethylstilbestrol, 0 1 to 1 0 mg by mouth daily, or ethinyl estradiol (Estinyl), 0 02 to 0 05 mg once a day according to the needs of the patient, is effective in these cases

Headache is often a serious problem and may continue in spite of all therapeutic measures The Rauwolfia compounds often relieve headache in addition to their pressure-lowering effects Phenobarbital, as already outlined, frequently helps If adjunctive therapy is required for headaches, the simpler measures should be tried first A morning headache will often be relieved by a cup of hot coffee or tea on awakening A simple procedure such as soaking the feet and legs in water as hot as can be tolerated, 2 or 3 times a day for 30 minutes to an hour, or taking hot, soaking baths, occasionally gives relief Acetylsalicylic acid 0 3 or 0 6 gm every 3 hours is helpful Occasionally the addition of codeine phosphate 30 to 60 mg at 3 or 4 hours intervals, is required Sometimes repeated lumbar puncture, to maintain a nearly normal cerebrospinal fluid pressure, is necessary For many years one of us has had excellent results in the treatment of hypertensive headaches by the use of a mixture of equal parts of elixir potassium thiocyanate and elixir of phenobarbital, one teaspoonful 3 times a day after meals, and an additional teaspoonful at bedtime if the headaches are severe or if morning headaches are particularly troublesome Curiously, this mixture rarely causes toxic symptoms and, on the above dosage gives blood thiocyanate levels of 6 to 10 mg per cent quite consistently

Sympathectomy, when properly performed on well selected patients,

tion that precipitates the symptoms either at work at play or during sleep In many cases the patient sleeps with the arms overhead and must be taught to keep the arms at the side during rest This may be facilitated by making a nest of 3 small pillows the first placed transversely the other two obliquely from above downward and outward, with the patient s neck and shoulders in the nest This throws the shoulders forward and often gives considerable relief In more severe cases surgical correction of an anatomical defect may become necessary such as scalenotomy or removal of the first rib or a cervical rib

BIBLIOGRAPHY

1 ALLEN E V BARKER, N W and HINES E A JR *Peripheral Vascular Diseases,* W B Saunders Co Phila 1948

2 ARMBRUST C A JR and LEVINE S A 'The Treatment of Angina Pectoris with a Preparation of Khellin (Ammi visnaga)' *Am Jour Med Sc* 1950 ccxx, p 127

3 BARKER N W Hypertension and Unilateral Renal Disease *Med Clin No Amer*, July 1951 p 1041

4 BEYER, J A, and WRIGHT I S 'The Hyperabduction Syndrome with Special Reference to Its Relationship to Raynaud s Syndrome *Circulation* 1951 iv, No 2 p 161

5 BLUMGART H L FRIEDBERG A S and KURLAND G S Treatment of Incapacitated Euthyroid Cardiac Patients by Producing Hypothyroidism with Radioactive Iodine *N E J Med* 1951 ccxlv p 83

6 DeTAKATS G Diagnosis and Management of Peripheral Vascular Disease *Med Clin No Amer*, January 1952 p 141

7 DOCK W Causes of Arteriosclerosis *Bull N Y Acad Med* 1950 xxvi p 182

8 GOFMAN J W JONES H B LINDGREN F T LYON T P ELLIOTT H A and STRISOWER BEVERLY 'Blood Lipids and Human Arteriosclerosis *Circulation*, 1950 ii p 161

9 GROLLMAN A Sodium Restriction in the Diet of Hypertension *Jour Am Med Assoc* 1945 cxxix p 533

10 HELLERSTEIN H K and BROFMAN B L The Treatment of the Hypotensive State Accompanying Myocardial Infarction *Mod Concepts Card Vasc Dis* Aug 1951 xx No 8

11 HUPPER W C Prevention and Treatment of Arteriosclerosis *Med Clin No Amer*, May 1949 p 773

from renal ptosis with possible renal ischemia Treatment consists of wearing a corset with a pad arranged to hold up the ptosed kidney Rarely nephropexy may be helpful

Hypotension

Although not strictly a disease entity, low blood pressure does produce symptoms that occasionally are severe enough to require relief It may occur as essential hypotension without any known cause, it may occur secondary to other debilitating diseases, or it may follow sympathectomy for hypertension It may be postural or orthopedic in type, with marked fall in blood pressure occurring when the patient stands Every effort must be made to improve the patient's general condition Fresh air, nourishing diets, carefully regulated and graded exercise, ample rest, and cool baths or showers with brisk rub downs are all helpful Infections and other diseases should be sought for and adequately treated Relief from an anemia or infection will often produce a striking improvement in the hypotension

Abdominal supports with pressure pads are useful In severe cases of the postural variety, elastic bandages on the legs may help until other measures become effective Elevation of the head on pillows or raising the head of the bed during sleep is occasionally helpful

Hydroxyamphetamine (Paredrine) hydrobromide, 20 to 40 mg by mouth 3 times a day, or phenylephrine (Neosynephrine) hydrochloride, 10 to 25 mg orally repeated as indicated by the patient's needs, is useful and frequently gives temporary relief Ephedrine sulfate, 25 to 50 mg by mouth 3 times a day, is useful when a more prolonged hypertensive action is desired Occasionally amphetamine (Benzedrine) sulfate, 5 to 10 mg by mouth once or twice a day, is useful if there is mental depression or drowsiness Hypotension appearing with hunger and a low blood sugar is discussed elsewhere

Hyperabduction Syndrome

The several neurovascular syndromes that fall into this category, including cervical rib syndrome, scalenus anticus syndrome, and shoulder bursa phenomenon, often have a large element of subclavian artery compression that may give Raynaud's symptoms and yet must be differentiated carefully from Raynaud's peripheral spastic phenomenon The treatment should be directed primarily toward elimination of the posi

28 MILLER A J and BAKER C A L arterenol (Levophed) in the Treatment of Shock Due to Acute Myocardial Infarction *Arch Int Med*, 1952 LXXXIX p 591
29 KURLAND G S and MALACH M The Clinical Use of Nor Epinephrine in the Treatment of Shock Accompanying Myocardial Infarction and Other Conditions *N E J Med*, 1952 CCXLVII p 383
30 O HARE J P and HOLDEN R B Longevity in Benign Essential Hypertension *Jour Amer Med Assoc*, 1952 CXLIX p 1453
31 FRANCKE D E Hospital Formulary of Selected Drugs, U Mich Hosp Hamilton Press Hamilton, Ill 1954
3 SCHROEDER H A MORROW J D and PERRY H M Jr Studies on the Control of Hypertension by Hyphex I Effects on Blood Pressure *Circulation*, 1953 VIII 672 II Toxic Reactions and Side Effects *Circulation*, 1953 VIII, 829 V Effects on the Course of the Malignant Stage *Circulation*, 1954 X 321
33 WILKINS R W *Combinations of Drugs in the Treatment of Hypertension* Mississippi Doctor April, 1953 359
34 GRIMSON K S Drugs Recently Introduced for Hypertension *J A M A*, 1955, CLVIII 359
35 KAHN E A 'Twenty Years Experience with Surgery of Hyper tension *N E J Med* 1954 CCLI 633

12 IRVIN, C W JR, and BURGESS, A M JR "Abuses of Bed Rest in Treatment of Myocardial Infarction," *N E J Med*, 1950, CCXLIII p 486

13 KEMPNER, W Some Effects of Rice Diet Treatment of Kidney Disease and Hypertension" *Bull N Y Acad Med*, 1946 XXII, p 358

14 MELLINKOFF, S M MACHELLA, T E, and REINHOLD J G 'Effect of Fat-free Diet in Causing Low Serum Cholesterol," *Am. Jour Med Sc*, 1950, CCXX, p 203

15 PAGE I H 'Treatment of Essential and Malignant Hypertension," *Jour Amer Med Assoc*, 1951, CXLVII, p 1311

16 RUSSEK, H I, ZOHMAN, B L, WHITE, L G, and DOERNER, A A Indications for Bishydroxycoumarin (Dicumarol) in Acute Myocardial Infarction' *Jour Amer Med Assoc*, 1951, CXLV, p 390

17 RYTAND D A 'Anticoagulants in Coronary Thrombosis with Myocardial Infarction" *Arch Int Med*, 1951, LXXXVIII p 207

18 SAMPSON J J and SINGER, I M 'Plasma and Blood Infusion Following Myocardial Infarction, *Am Heart Jour*, 1949 XXXVIII, p 54

19 SILBER, E N, LEVIN B D, BECKER G H, and LEVY, R C Treatment of Shock of Recent Myocardial Infarction by Intra arterial Transfusion," *Jour Amer Med Assoc*, 1951 CXLVII, p 1626

20 SMITHWICK, R H Splanchnicectomy in Hypertensive Cardio-vascular Disease," *Jour Amer Med Assoc*, 1951, CXLVII p 1611

21 SMITHWICK, R H Surgical Treatment of Continued Hypertension Some Suggestions About Selection of Cases for This Form of Therapy *J Med Soc N J*, 1947, XLIV, p 304

22 WAITZKIN, L Treatment of Angina Pectoris with Propylthiouracil" *Ann Int Med*, 1951, XXXIV, p 1107

23 WAKERLIN G E "Pathogenesis and Treatment of Essential Hypertension' *Med Clin No Amer*, January 1952 p 1 9

24 WELLMAN W E, and ALLEN E V 'The Variable Effects of Identical Amounts of Dicumarol on the Prothrombin Values of Different Persons" *Proc Staff Meet Mayo Clinic*, 1951 XXVI, p 257

25 WHITE, P D, BRIDGES, M C and WHEELER, E O "Low Sodium and Free Water Intake in Treatment of Congestive Heart Failure *Tr A Am Physicians*, 1946 LIX, p 53

26 WINSOR T and HUMPHREYS P Influence of Pentaerythritol Tetranitrate (Peritrate) on Acute and Chronic Coronary Insufficiency" Angiology, 1952 III p 1

27 WRIGHT, I S The Modern Treatment of Coronary Thrombosis with Myocardial Infarction *Circulation*, 1950, II p 929

cava, usually little can be done In carefully selected cases a wiring operation may be successful If the aneurism is due to syphilis attempts to prevent further enlargement by careful antisyphilitic treatment so as to avoid a Jarisch Herxheimer reaction may be instituted as outlined in the section on Syphilis

In the lower torso obstruction to venous blood flow in the inferior vena cava may be due to pelvic or abdominal tumors which should be removed if possible but more commonly it is due to phlebitis and thrombosis which frequently extend upward from pelvic thrombophlebitis This type will be considered more extensively under venous thrombosis

Thrombophlebitis and Phlebothrombosis

There may be some merit for considering intravenous vascular clotting under two headings thrombophlebitis and phlebothrombosis, because (1) there are certain differences early in the pathology of the two conditions, (2) since phlebothrombosis may have few or no symptoms constant vigilance is required for its recognition in order that proper therapy may be instituted to prevent catastrophic pulmonary embolism (3) phlebothrombosis particularly of the pelvic veins and the deep veins of the lower extremities is a more common source of pulmonary embolism than is thrombophlebitis Some feel however that after several days of the thrombotic process, there is little distinction to be made between the two One cannot predict that an embolus will not occur From the standpoint of treatment the following facts remain (1) venous thrombosis may be quite asymptomatic and must be suspected and watched for constantly in order to institute proper therapy, (2) superficial vein involvement is more likely to be painful than deep vein thrombosis the latter referring particularly to thrombosis of femoral and pelvic veins (3) deep venous thrombosis primarily of the calf and pelvis is much more likely to be the source of emboli to the heart or to the lungs than is thrombosis of superficial veins and the veins of the thigh or of the arms

In the following discussion the term thrombophlebitis will be used to designate both conditions It may be considered arbitrarily under the headings (1) primary (2) secondary and (3) septic thrombophlebitis

Primary Thrombophlebitis

In primary thrombophlebitis no etiological cause is apparent as it is in cases with antecedent injury infection operation obstetrical delivery

CHAPTER LXIV

DISEASES OF THE VEINS

Diseases of the veins and disturbances of the venous blood flow may be divided into (1) obstructive diseases, external and internal, which include compression from tumors, swellings, aneurisms, obstruction from thrombosis, neoplastic invasion, and pulmonary embolism, (2) nonobstructive diseases, which include varicose veins and arteriovenous fistulae, (3) acute and chronic venous insufficiency, which may result from several of the conditions listed above, and (4) tumors of the blood vessels, telangiectases and hemangiomata

Obstruction Due to External Compression

A good example of this type is obstruction of the superior and sometimes the inferior vena cava Mediastinal tumors, such as lymphomas, fibrosis aortic aneurisms, and constrictive pericarditis, can cause obstruction of venous return to the right auricle by external pressure, with passive congestive phenomena of the head, neck, upper extremities, and thorax In the upper torso localized enlargement of lymph nodes in the neck or in the axillae may give rise to local venous compression phenomena Statistics have shown that, when such compression of venous flow is due to a tumor, the neoplasm is usually malignant, highly invasive, and always potentially serious If readily accessible, such tumor masses in the neck or axillae should be excised When the compressing tumor is in the mediastinum or thorax high voltage x ray therapy can be tried but this should be done with caution lest the reaction to irradiation be one of edema and swelling with an increase in venous compression On the other hand, extremely radio sensitive lymphomata may shrink rapidly under such roentgen therapy When fibrosis can be established as the cause of the venous obstruction, roentgen therapy should be avoided and surgical dissection attempted Skilful surgical exploration of the thorax is becoming increasingly successful For an aneurism of the aorta large enough to compress the superior vena

failure Anticoagulant therapy has been shown to be beneficial by the diminution of complications in patients with coronary thrombosis and by the prevention of thrombophlebitis and pulmonary embolism in many cases of auricular fibrillation and heart failure

Proper treatment of the causative factors just outlined by the use of anticoagulants by adequate nutrition by maintaining fluid and electrolyte balance, and by reasonably early ambulation and activity of the patient will go far in preventing thrombophlebitis At all times marked sedation should be avoided The incidence of thrombophlebitis and thromboembolism following surgery or delivery is too small to warrant the routine use of anticoagulants in surgery or obstetrics. When anticoagulants are indicated however as in cases with a past history of phlebitis or embolism and after abdominal and pelvic surgery they should be used they should not be started until 48 hours after the operation or 8 days after delivery when the uterus is well involuted Other measures for the prevention of thrombophlebitis are given in Chapter 1

The immediate treatment of thrombophlebitis depends in part upon its location and in part upon its cause *Local thrombophlebitis* occurs most commonly after the intravenous injection of drugs or solutions which injure the intima of the vein The thrombophlebitis following intravenous administration of drugs for systemic effect can be avoided by using the oral or intramuscular route of administration In general practice intravenous medication is frequently overdone When a reaction occurs an ice bag applied to the part and kept on for an hour or two will aid greatly in relieving pain Ordinarily it is best not to apply cold to an area of thrombophlebitis for any considerable length of time as it will cause more spasm ischemia and possibly extension of thrombosis In such local lesions heat applied in the form of moist wet packs should be started within 4 hours and continued acetylsalicylic acid 0 6 gm every 4 or 6 hours or codeine phosphate 15 to 30 mg every 4 to 6 hours should be given as long as fever pain and swelling persist Fortunately thrombosis from an arm vein seldom causes pulmonary embolism When a localized thrombophlebitis in an arm as in the antecubital vein or in a leg is releasing multiple pulmonary emboli surgical ligation of the vein should be carried out

Local thrombophlebitis may occur spontaneously in a varicosed vein particularly of the leg As these are superficial and very irregular in their diameter the narrowed segment of vein proximal to the varicosity is usually in itself a guard against pulmonary embolism Rest to the part a moderately firm bandage and the measures outlined in the preceding

CHAPTER LXIV

DISEASES OF THE VEINS

Diseases of the veins and disturbances of the venous blood flow may be divided into (1) obstructive diseases, external and internal, which include compression from tumors, swellings, aneurisms, obstruction from thrombosis neoplastic invasion, and pulmonary embolism, (2) non obstructive diseases which include varicose veins and arteriovenous fistulae, (3) acute and chronic venous insufficiency, which may result from several of the conditions listed above, and (4) tumors of the blood vessels, telangiectases, and hemangiomata

Obstruction Due to External Compression

A good example of this type is obstruction of the superior and sometimes the inferior vena cava Mediastinal tumors, such as lymphomas, fibrosis, aortic aneurisms, and constrictive pericarditis, can cause obstruction of venous return to the right auricle by external pressure, with passive congestive phenomena of the head, neck, upper extremities, and thorax In the upper torso localized enlargement of lymph nodes in the neck or in the axillae may give rise to local venous compression phenomena Statistics have shown that, when such compression of venous flow is due to a tumor, the neoplasm is usually malignant, highly invasive and always potentially serious If readily accessible, such tumor masses in the neck or axillae should be excised When the compressing tumor is in the mediastinum or thorax, high voltage x ray therapy can be tried but this should be done with caution lest the reaction to irradiation be one of edema and swelling with an increase in venous compression On the other hand extremely radio sensitive lymphomata may shrink rapidly under such roentgen therapy When fibrosis can be established as the cause of the venous obstruction, roentgen therapy should be avoided and surgical dissection attempted Skilful surgical exploration of the thorax is becoming increasingly successful For an aneurism of the aorta large enough to compress the superior vena

stasis, not much benefit would be derived from sodium deprivation but the administration of excessive sodium chloride should be avoided Fluids should be given freely as indicated by the desire of the patient

Blocking of regional sympathetic ganglions with procaine hydro chloride may by release of associated arterial spasm increase local blood flow to the part and thereby aid in subsidence of edema This will be considered in this chapter under Surgical Treatment

With adequate kidney function early in the course of acute throm bophlebitis the use of mercurial diuretics such as mercaptomerin (Thiomerin) 1 to 3 cc subcutaneously on every second or third day, may prove helpful in relieving localized edema and in reducing pain and discomfort from the compressing effect of the edema, it is worthy of trial It is important not to allow such diuresis to cause any general dehydration

The authors feel that it is highly important to keep the degree of edema at an absolute minimum during the course of an acute throm bophlebitis in an extremity *Proper control of the edema goes far in* reducing the probability of a later chronically swollen leg Chronic swelling may be avoided by proper control of edema while skin elas ticity is still intact This means that the edema should be controlled at the very beginning of treatment of acute thrombophlebitis certain studies have suggested that after 3 months of persistent edema chronic edema tends to result

In addition to the measures already outlined as edema subsides, an elastic bandage should be applied to maintain the advantages that have been gained Not until all pain swelling fever and other constitutional symptoms have subsided should *activity of the part be allowed and then* only with the protection of an elastic stocking

Anticoagulant Therapy There is no doubt at the present time of the beneficial effect of adequate anticoagulant therapy in preventing propagation of a thrombus and of embolic phenomena In uncomplicated thrombophlebitis following the initial determination of the blood prothrombin time the patient should be given 300 mg of bishydroxy coumarin (Dicumarol) as a single dose during the first 24 hours (00 *mg if the weight is less than 150 pounds) followed by 200 mg the* second day 100 mg the third day with an average daily maintenance dose of 50 to 100 mg to keep the prothrombin time in seconds about double that of the control (15 to 30 per cent) This level should be maintained for 14 to 1 days If embolic phenomena have already oc curred treatment should be initiated immediately Heparin, 50 mg

constitutional disease, or blood dyscrasia It may be part of the picture in thromboangiitis obliterans, occurring at some time in as many as 40 per cent of these cases It may be recurrent in various locations in the body, to which the name idiopathic recurrent thrombophlebitis or phlebitis migrans has been given The latter may be a manifestation of carcinomas, particularly of the pancreas or lung, in these, enzymes may play a causative part, but neoplastic cells in the veins do not

The treatment for this condition is the same as outlined under Secondary Thrombophlebitis in the following paragraphs In addition, foci of infection in the teeth, tonsils, ear, prostate, or cervix should be removed in an attempt to improve the physical health of the individual as well as to remove possible causative factors Such an approach has been found to be worth while

Secondary Thrombophlebitis

This is by far the most frequently occurring type, in which the venous thrombosis occurs during the course of, or following, local trauma, local and systemic infections, post operative or post partum heart disease with heart failure, blood dyscrasia, and long continued bed rest carried out for any reason, particularly in the presence of debility

In the treatment of secondary thrombophlebitis all of the causative conditions given above should be corrected if possible Proper immobilization with a minimum of further trauma in the care of the fractured extremity will aid greatly in minimizing phlebitis Any infection local or systemic, should be treated adequately with chemotherapy, antibiotics and other appropriate measures, depending upon the infection and its location Surgical operation especially in the abdomen or pelvis, is likely to be followed by thrombophlebitis This tendency is definitely increased by the presence of obesity, anemia, cancer, heart disease severe infection or long continued bed rest Early ambulation after operation is not the completely preventive measure it was once hoped to be, but it is helpful in this connection In obstetrical delivery the same factors obtain as already given for surgical operations The use of elastic bandages or elastic stockings for the legs of bed patients helps maintain a more adequate blood flow and may prevent stasis and possible thrombus formation

A great many cases of thrombophlebitis occur during the bed rest therapy carried out for heart disease particularly in patients with cardiac

stasis not much benefit would be derived from sodium deprivation but the administration of excessive sodium chloride should be avoided Fluids should be given freely as indicated by the desire of the patient

Blocking of regional sympathetic ganglions with procaine hydro chloride may by release of associated arterial spasm increase local blood flow to the part and thereby aid in subsidence of edema This will be considered in this chapter under Surgical Treatment

With adequate kidney function early in the course of acute thrombophlebitis the use of mercurial diuretics such as mercaptomerin (Thiomerin) 1 to 3 cc subcutaneously on every second or third day may prove helpful in relieving localized edema and in reducing pain and discomfort from the compressing effect of the edema it is worthy of trial It is important not to allow such diuresis to cause any general dehydration

The authors feel that it is highly important to keep the degree of edema at an absolute minimum during the course of an acute throm bophlebitis in an extremity Proper control of the edema goes far in reducing the probability of a later chronically swollen leg Chronic swelling may be avoided by proper control of edema while skin elas ticity is still intact This means that the edema should be controlled at the very beginning of treatment of acute thrombophlebitis certain studies have suggested that after 3 months of persistent edema chronic edema tends to result

In addition to the measures already outlined as edema subsides an elastic bandage should be applied to maintain the advantages that have been gained Not until all pain swelling fever and other constitutional symptoms have subsided should activity of the part be allowed and then only with the protection of an elastic stocking

Anticoagulant Therapy There is no doubt at the present time of the beneficial effect of adequate anticoagulant therapy in preventing propa gation of a thrombus and of embolic phenomena In uncomplicated thrombophlebitis following the initial determination of the blood prothrombin time the patient should be given 300 mg of bishydroxycoumarin (Dicumarol) as a single dose during the first 24 hours (200 mg if the weight is less than 150 pounds) followed by 200 mg the second day 100 mg the third day with an average daily maintenance dose of 50 to 100 mg to keep the prothrombin time in seconds about double that of the control (15 to 30 per cent) This level should be maintained for 14 to 21 days If embolic phenomena have already oc curred treatment should be initiated immediately Heparin, 50 mg,

paragraph will usually suffice If suppuration occurs, excision of the thrombus should be carried out

Axillary thrombophlebitis following unusual effort or strain of the abducted arm or injury from the use of a crutch is still another form of localized phlebitis It should be treated with complete immobilization of the shoulder arm, and hand on the involved side, with continuous moist heat applied in the axilla and the administration of anticoagulants as described in the following paragraph Since pulmonary embolism occurs infrequently with this form of thrombosis, surgical ligation of the axillary or subclavian vein should not be done, in fact such treatment may make the edema of the upper extremity worse

The most frequent form of thrombophlebitis occurs in the legs and pelvis It is well to consider the thrombotic process to be more extensive than is apparent, for such is often the case

Medical Treatment Rest and elevation of the part are the first essentials in the conservative management of thrombophlebitis The application of tight binders, exercises, and the increasing activity advocated by a few in the past are not advised by the authors, these practices have been made even more obsolete by the introduction of anticoagulant therapy Bandaging the legs with elastic bandages or snugly fitting elastic stockings is a helpful measure, however, and does augment circulation in limbs and perhaps prevents spread

The patient should be kept at rest and the part elevated It has been found that a semi-Trendelenburg position, with the body straight, without flexion of the knees or hips and with the foot of the bed elevated 10 to 12 inches, and with 3 pillows under the patient s head, not only will aid in getting rid of edema but is also a factor in lessening the incidence of embolism During the acute, painful, edematous phase when there is severe inflammation, the entire calf or, if the lesion is not sharply localized the entire leg should be covered with cold cream or vaseline, and moist heat should be applied continuously This may be done with turkish towels or a thin blanket wrung out with hot water and wrapped loosely around the extremity, with hot-water bottles laid along the outside Obviously great care is needed to avoid a skin burn The leg should be covered for 18 to 20 out of the 24 hours and allowed to aerate for the remaining time As improvement occurs, such applications may be gradually lessened but they should be *continued as needed to control* the local inflammation During this *time adequate nourishment* fluids, and electrolytes must be given *as outlined in Chapter 1*

Since the edema of thrombophlebitis is caused by inflammation and

Vein ligation is recommended when anticoagulant therapy is contraindicated, as in purpura in certain cases of hepatic or renal disease in the presence of open lesions that may bleed or in the immediate postoperative period Vein ligation is indicated also when there is septic phlebitis when it can be demonstrated that the popliteal or femoral vein contains a thrombus and when the peripheral thrombotic process responsible for an episode of pulmonary embolism is within the leg or thigh When one embolus has occurred ligation is unquestionably the ideal prophylactic procedure On the other hand when emboli are arising from veins other than those in the thigh or calf an ill advised femoral vein operation is worse than useless Both vein ligation and anticoagulant therapy have their advantages and their shortcomings and they should be used in a balanced manner to supplement each other

In the experience of many physicians neither venous interruption nor the use of anticoagulants has entirely prevented pulmonary embolism The best treatment for the majority of patients therefore is to carry out all reasonable methods of prophylaxis

Septic Thrombophlebitis

The treatment of septic thrombophlebitis should be surgery together with proper antibacterial chemotherapy When possible the vein should be ligated at a point proximal to the involved segment The invading organism should be isolated by blood culture and the proper antibiotic or chemotherapeutic agent applied In some circumstances such as with septic cavernous sinus thrombosis it is advisable to institute anticoagulant therapy together with antibiotics

SEQUELAE OF THROMBOPHLEBITIS

The sequelae of thrombophlebitis include pulmonary embolism varicose veins (acute and chronic) venous insufficiency and stasis ulcers Many consider these part of the thrombophlebitic disease process

Varicosities of superficial veins often form following deep venous thrombosis as collateral circulation develops After recanalization of the deep veins has occurred the varicosities then become complications When in a year or two all evidence of activity of the thrombophlebitis has disappeared and canalization has occurred the varicose superficial saphenous veins and their branches should be treated as discussed in the following section

paragraph will usually suffice If suppuration occurs, excision of the thrombus should be carried out

Axillary thrombophlebitis following unusual effort or strain of the abducted arm or injury from the use of a crutch is still another form of localized phlebitis It should be treated with complete immobilization of the shoulder, arm, and hand on the involved side, with continuous moist heat applied in the axilla and the administration of anticoagulants as described in the following paragraph Since pulmonary embolism occurs infrequently with this form of thrombosis, surgical ligation of the axillary or subclavian vein should not be done, in fact such treatment may make the edema of the upper extremity worse

The most frequent form of thrombophlebitis occurs in the legs and pelvis It is well to consider the thrombotic process to be more extensive than is apparent, for such is often the case

Medical Treatment Rest and elevation of the part are the first essentials in the conservative management of thrombophlebitis The application of tight binders, exercises, and the increasing activity advocated by a few in the past are not advised by the authors, these practices have been made even more obsolete by the introduction of anticoagulant therapy Bandaging the legs with elastic bandages or snugly fitting elastic stockings is a helpful measure, however, and does augment circulation in limbs and perhaps prevents spread

The patient should be kept at rest and the part elevated It has been found that a semi-Trendelenburg position with the body straight, without flexion of the knees or hips and with the foot of the bed elevated 10 to 12 inches and with 3 pillows under the patient's head, not only will aid in getting rid of edema but is also a factor in lessening the incidence of embolism During the acute, painful, edematous phase when there is severe inflammation, the entire calf or if the lesion is not sharply localized the entire leg should be covered with cold cream or vaseline, and moist heat should be applied continuously This may be done with turkish towels or a thin blanket wrung out with hot water and wrapped loosely around the extremity, with hot-water bottles laid along the outside Obviously great care is needed to avoid a skin burn The leg should be covered for 18 to 20 out of the 24 hours and allowed to aerate for the remaining time As improvement occurs such applications may be gradually lessened but they should be continued as needed to control the local inflammation During this time adequate nourishment fluids and electrolytes must be given as outlined in Chapter 1

Since the edema of thrombophlebitis is caused by inflammation and

orders as hyperthyroidism uncontrolled diabetes mellitus extreme obesity and any blood diseases except mild hypochromic anemia varicose veins should not be injected Any obvious cause of venous obstruction such as an abdominal tumor should be removed before injections are given Varicose veins that develop during gestation should not be injected unless they persist after delivery During pregnancy furthermore quinine preparations should not be used in the injection solution lest they cause abortion

Of the various sclerosing solutions used at the present time sodium morrhuate in 5 per cent solution and sodium ricinoleate solution (Soricin Sclerosing Solution 2 per cent) are the most popular Quinine and urethane U S P is irritating and gives an occasional serious reaction it has largely been replaced by sodium morrhuate and sodium ricinoleate The first injection of sodium morrhuate should be a test dose 0 5 to 1 0 cc locally into a small varicose vein 12 to 24 hours before a course of treatment is expected to be given A reaction is manifested by the occurrence of a diffuse erythema followed by generalized pruritus This occurs most commonly in patients who have various types of allergy and contraindicates further injections of the drug If no reaction occurs to the test dose the patient should be given 2 to 4 cc of sodium morrhuate every day for 8 to 10 days After each injection a sterile gauze pad should be applied firmly over the site with moderate pressure by means of a small bandage or adhesive tape The operation is facilitated by having the patient stand on the examining table 30 to 36 inches above the floor with something to grasp with his hands to prevent falling The injection is made upward in the vein with constrictions applied to the vein above the site of injection

If sodium morrhuate is not desired or a reaction develops to the test dose sodium ricinoleate solution (Soricin Sclerosing Solution 2 per cent) may be employed A test dose of 0 5 cc into a small varicosity is made 4 or 5 days before actual treatment is begun If no reaction occurs 1 0 to 2 0 cc of the solution is injected intravenously to obliterate localized varicosities Doses from 2 to 5 cc may be required to obliterate more extensive varicosities such as the trunk of the great saphenous vein No more than 8 0 to 10 0 cc should be used at any one time in injecting multiple sites Treatments may be repeated at weekly intervals Care must be exercised to avoid extravascular injection as the solution is highly irritating to tissue and sloughing may ensue The technique of injection and after treatment is the same as that recommended for sodium morrhuate

should be given intravenously every 3 or 4 hours or as a continuous drip for the first 24 to 48 hours while at the same time bishydroxycoumarin therapy is instituted as just outlined With embolic phenomena, some combine femoral vein ligation with anticoagulant therapy, others prefer vein ligation to anticoagulant therapy Femoral vein ligation is discussed in this chapter under Surgical Treatment

The proper treatment of acute thrombophlebitis requires early recognition of the condition and meticulous attention to the details of treatment The treatment should be continued long enough to insure complete recovery and the prevention of chronic milk-leg

The treatment of recurring acute thrombophlebitis is the same as that outlined for the initial attack The therapy of chronic thrombophlebitis is essentially that for its complications varicose veins, chronic vascular insufficiency and indolent ulcers which are considered later under those headings

Surgical Treatment In the acute phase of thrombophlebitis, when there is evidence of associated arterial spasm paravertebral sympathetic block may be helpful in relieving pain and in lessening edema Such therapy requires skilled hands however, for regional anesthesia is difficult and should not be attempted by the novice As a routine procedure in treatment it has not met with universal success

Venous Ligation Thrombophlebitis presents a group of syndromes in which the involvement is usually more extensive and widespread than is expected Thus in iliofemoral thrombosis the process not infrequently extends into the pelvic veins and into the veins of the other leg Furthermore since embolism from thrombosed varicose veins, such as the long saphenous vein is unusual routine ligation of the long saphenous vein accomplishes little in the prevention of pulmonary embolism For those reasons venous ligation has not been accepted as a routine treatment for all cases of thrombophlebitis of the leg, although it has a very definite place When emboli continue to occur in spite of adequate anticoagulant treatment femoral vein ligation is advisable The difficulty consists in knowing from which leg the emboli are originating and whether the process already extends above the ilioinguinal ligament When thrombophlebitis localized in the deep veins of the calf has caused embolism femoral vein ligation is indicated If the thrombophlebitis is largely in the pelvic veins and is extending upward ligation of the inferior vena cava probably should be carried out, but with the likelihood of resultant subsequent chronic edema of the lower torso and extremities Proper venous ligation however can be life saving

effect An elastic stocking overcomes the latter but has not the advantages of the former The stocking should extend from well above the knee to the toes adequately covering the ankle and should be held up by garters fastened to a girdle or abdominal stay

As a result of nutritional disturbances of the tissues from chronic venous insufficiency various forms of *eczema* and *indurated cellulitis* develop in the involved leg When either of these occurs treatment should be begun with complete bed rest and elevation of the leg Only bland non irritating ointments should be applied to an eczematous skin, such as 3 per cent ichthyol in zinc oxide to allay itching The patient must refrain from scratching the lesions For acute cellulitis elevation of the leg and the application of warm boric acid soaks will be helpful Associated varicose veins should be eliminated by sclerosing solution ligation or both

Stasis Ulcer

When stasis ulcer occurs the most effective treatment is elevation and complete immobilization of the leg and meticulous cleanliness of the ulcerated area Begin with boric acid soaks penicillin parenterally or orally in adequate do age and the application of bacitracin ointment if there is infection Frequently, small varicosed veins surround the area and these should be eliminated by sclerosis In the last stages incompe tence of arterioles with poor healing is frequently present for which vitamin C 300 mg daily by mouth may be helpful Other measures that may be tried include the use of a rubber sponge applied firmly over the ulcer and held in place by an elastic bandage or when edema is not present, an Unna paste boot changed every 5 to 10 days

Unna s Paste

Zinc oxide	1000 gm
Gelatin	600 gm
Glycerin	1400 cc
Distilled water	2200 cc

With a large intractable or deep ulcer much time and discomfort may be saved by performing a split skin graft after excision of the ulcer area

Arteriovenous Fistula

Arteriovenous fistulae are either (1) congenital or (2) acquired

The treatment of *congenital* arteriovenous fistula or aneurism is

Varicose Veins

A varicose vein results when a segment or an entire length of a vein is dilated Ordinarily the condition of varicose veins refers to involvement of the superficial veins of the lower extremities Other types of varicose veins, sometimes referred to as phlebectasis, are seen with arteriovenous aneurisms and certain tumors of blood vessels

Varicose veins of the legs are of two types (1) primary, in which there is a defect in the valves or the wall of the vein, and (2) secondary, occurring as a compensatory phenomenon in thrombophlebitis and as a result of back pressure in pregnancy, abdominal tumors, and other obstructive conditions

The treatment of primary varicose veins and of many cases of the secondary type, after the obstructive cause has been removed, may be considered in 3 categories (1) conservative therapy, (2) obliteration with sclerosing solutions, and (3) surgical ligation

Conservative Therapy The conservative therapy for varicose veins should be limited to those cases in which the varicosities are mild or in which more radical treatment would be contraindicated because of age or some chronic illness, particularly an illness with a poor prognosis Conservative treatment consists of adequate periods of rest with the legs elevated careful avoidance of excessive standing or unnecessary walking and the application of an elastic (Ace) bandage or a light elastic stocking for support The function of such support is to force the stagnant, superficial, venous circulation into the deep veins for return flow to the heart With or without treatment, thrombophlebitis has a tendency to develop in the stagnant dilated veins

Obliteration with Sclerosing Solutions The obliteration of varicose veins by means of injecting a sclerosing solution directly into them was practiced extensively a few years ago At the present time it is considered chiefly as a form of therapy adjuvant to the use of surgical ligation and stripping of the vein with removal if necessary

There are certain contraindications to the injection treatment of varicose veins including old age or any disease that carries a poor prognosis such as severe cardiac disease, malignancy and marked debility Acute infections, particularly an acute cellulitis, lymphangitis, or pyogenic infection of the affected extremity militate against injection Further the veins of an extremity should not be so treated if there is occlusive arterial disease or recent thrombophlebitis involving the deep veins of the thigh or leg In the presence of such constitutional dis

Spider nevi are seen in patients with liver disease in pregnant women in people with vitamin B deficiency and occasionally in normal individuals Recent evidence indicates a relation to an increase in circulating estrogens Spider nevi are to be distinguished from petechiae a differentiation easily determined by the fact that the nevi will disappear with pressure under a glass slide For cosmetic reasons they may be removed by electrolysis cautery puncture or injection of minute amounts of a sclerosing solution such as sodium morrhuate 5 per cent into the central vessel Usually no treatment is required and they rarely bleed

Senile vascular nevi are to be treated in the same way as spider nevi

Congenital telangiectasia characterized by groups of dilated capillaries, especially on the face and neck seldom cause difficulty If required treatment should consist of electrolysis but the peripheral vessels should be destroyed first and then destruction extended to the central area

Hereditary hemorrhagic telangiectasia is characterized by multiple small telangiectatic lesions of the skin and mucous membranes and by the tendency to hemorrhage The accessible lesions and particularly those in the nose because of the occurrence of frequent epistaxis should be treated with electrocoagulation Cautery chromic acid or other caustic should be applied to local superficial lesions some feel that radium is contraindicated As a prophylactic measure large doses of vitamin C and vitamin K may be helpful For severe bleeding and anemia transfusions of whole blood are indicated For bleeding from inaccessible telangiectasis such as may occur in the gastro intestinal tract the measures recommended for Hemophilia should be tried

Pulsating telangiectasis is the term used for large nevi that pulsate They occur rarely and bleeding from them is unusual Since they are often associated with active liver disease drugs and chemicals that may be hepatotoxic including alcohol should be avoided Careful search for liver involvement should be made and treatment for any liver disease should be carried out No specific treatment is required

Hemangioma is a more localized type of telangiectasia but unlike the latter which is usually acquired and occurs most commonly in adult life hemangioma is a form of congenital slow growing tumor of newly formed blood vessels There are various types of hemangiomata the port wine stain the strawberry nevus the cavernous hemangioma the diffuse hemangioma the cirsoid aneurism and the congenital arteriovenous fistula

Surgical Ligation For primary varicose veins the majority of patients are benefited by division of the great saphenous vein at the saphenofemoral junction, with concomitant injection of the distal segment with a sclerosing solution If the varicosities are huge, multiple ligations may be preferable similarly combined with injection of adjoining segments If only the small or short saphenous system is involved, injections treatment alone may be sufficient

Single or multiple ligation of varicose veins is a formidable procedure and is not to be considered as a minor office technique Full operating room equipment should be utilized, with careful asepsis

Superficial thrombophlebitis, a local chemical phlebitis, is the desired consequence of the injection procedure When no irritants have been applied however a thrombophlebitis may occur spontaneously in superficial varicose veins Such a complication is to be treated as outlined under Thrombophlebitis

Venous Insufficiency

Venous insufficiency may be acute or chronic The relatively rare *acute* form involves arterial as well as venous circulation and occurs in the course of acute venous thrombosis It is also spoken of as acute peripheral circulatory failure There is shock, with marked drop in blood pressure weak rapid pulse cold, moist skin, and increased swelling of the involved limb Transient extra-renal azotemia may occur Treatment for this reaction should consist of the administration of oxygen blood transfusions and management for shock

Chronic venous insufficiency is characterized by edema, at first soft and pitting later brawny dusky cyanosis, prominence of superficial veins and in rare cases, skin changes with ulceration, particularly on the medial aspect of the ankle The patient should be kept off his feet, the foot of the bed should be elevated 10 to 12 inches during sleeping hours and during daily rest periods which are advised to keep the leg as free from edema as possible If extensive varicose veins are present and if canalization of deep veins has occurred as evidenced by tests for adequacy of the deep venous circulation ligation should be done At times when the edema is minimal such as on arising and after a [illegible] hour rest, the involved extremity should be supported by an elastic (Ace) bandage or an elastic stocking An elastic bandage has the advantage of close application to the leg contour regardless of its size but it has also the disadvantage of slipping down and, in women, an unpleasant cosmetic

Spider nevi are seen in patients with liver disease in pregnant women, in people with vitamin B deficiency and occasionally in normal individuals Recent evidence indicates a relation to an increase in circulating estrogens Spider nevi are to be distinguished from petechiae a differentiation easily determined by the fact that the nevi will disappear with pressure under a glass slide For cosmetic reasons they may be removed by electrolysis cautery puncture or injection of minute amounts of a sclerosing solution such as sodium morrhuate, 5 per cent into the central vessel Usually no treatment is required and they rarely bleed

Senile vascular nevi are to be treated in the same way as spider nevi

Congenital telangiectasia characterized by groups of dilated capillaries especially on the face and neck seldom cause difficulty If required treatment should consist of electrolysis but the peripheral vessels should be destroyed first and then destruction extended to the central area

Hereditary hemorrhagic telangiectasia is characterized by multiple small telangiectatic lesions of the skin and mucous membranes and by the tendency to hemorrhage The accessible lesions and particularly those in the nose because of the occurrence of frequent epistaxis should be treated with electrocoagulation Cautery chromic acid or other caustic should be applied to local superficial lesions some feel that radium is contraindicated As a prophylactic measure large doses of vitamin C and vitamin K may be helpful For severe bleeding and anemia transfusions of whole blood are indicated For bleeding from inaccessible telangiectasis, such as may occur in the gastro intestinal tract the measures recommended for Hemophilia should be tried

Pulsating telangiectasis is the term used for large nevi that pulsate They occur rarely and bleeding from them is unusual Since they are often associated with active liver disease drugs and chemicals that may be hepatotoxic including alcohol should be avoided Careful search for liver involvement should be made and treatment for any liver disease should be carried out No specific treatment is required

Hemangioma is a more localized type of telangiectasia but unlike the latter, which is usually acquired and occurs most commonly in adult life hemangioma is a form of congenital slow growing tumor of newly formed blood vessels There are various types of hemangiomata the port wine stain the strawberry nevus the cavernous hemangioma the diffuse hemangioma the cirsoid aneurism and the congenital arteriovenous fistula

usually extremely difficult because of the multiplicity of vessels involved Treatment with radium may be of value when it can be applied to angiomatous areas over the large dilated vessels If a single artery and vein are involved primarily, surgical excision should be attempted Ligation of the artery proximal to the site of multiple communications, or simultaneous ligation of the artery and its accompanying veins, is usually of little value Subsequent amputation of an arm or leg often becomes necessary

In the presence of a fistula with multiple communications, particularly on an extremity, a satisfactory method of therapy is the application of rubber bandages to compress the abnormal veins, thereby aiding the blood to pursue a more normal arterial course

The treatment of *acquired* arteriovenous fistula, whether traumatic or arteriosclerotic should be removal of the communication by surgical closure This should be done for the prevention as well as for the relief of cardiac enlargement with myocardial insufficiency, and for chronic venous insufficiency with complicating varicose veins, stasis dermatitis, and ulceration When the patient's condition permits, the surgical closure may be performed at any time, although some feel that the optimum time is 3 to 6 months after the injury to allow for the development of adequate collateral circulation

Tumors of the Blood Vessels

The tumors of blood vessels considered here include the telangiectases such as glomus tumor, spider nevi, senile vascular nevi, hereditary hemorrhagic telangiectasis, pulsating telangiectasis, and the smaller, more localized forms designated as hemangiomata The latter may be malignant in which case the suffix endothelioma or sarcoma should be added to designate the type

Telangiectasia is a form of enlargement of capillaries and small vessels as seen in glomus tumors (glomangioma), the nevi associated with acne rosacea lupus erythematosus, xeroderma pigmentosa and excessive exposure of the skin to sun wind radium, or roentgen rays

Glomus tumor, often subungual is the only form of telangiectasia that is characterized by severe pain Treatment should be complete excision of the tumor Local anesthesia in patients with a glomus tumor may cause excessive constriction of blood vessels with resulting gangrene of the finger or toe

BIBLIOGRAPHY

1 ALLEN E V BARKER N W and HINES E A *Peripheral Vascular Diseases* W B Saunders Co., Phila 1948
2 BARROW D W Present Management of Varicose Veins *N E J, Med* 1951 CCXLIV p 321
3 COSGRIFF S W CROSS R J and HABIF D V 'The Management of Venous Thrombosis and Pulmonary Embolism *Surg Clin No Amer*, April 1948 p 324
4 DeTAKATS G The Management of Acute Thrombophlebitic Edema *Jour Amer Med Assoc*, 1933 C, p 34
5 DeTAKATS G The Management of Varicose Veins of the Lower Extremities *Surg Clin No Amer*, Oct 1951 p 1463
6 EDWARDS E. A Migrating Thrombophlebitis Associated with Carcinoma, *N E J Med*, 1949 CCXL, p 1031
7 SCHNITKER M A Use of Diuretics in the Treatment of Certain Localized Edemas *Ohio State Med Jour*, 1941 XXXVII, p 328
8 TRAUB E F Nevi *Med Clin No Amer*, March 1951 p 301

Treatment for a small localized hemangioma should be carried out as early in life as is reasonable. Even though spontaneous involution does occur in some cases, it should not be awaited, for as the child grows and develops, the hemangioma may develop arteriovenous connections and enlarge. Therapy should be the eradication of the lesion by a skilled specialist with either radium, electrocoagulation, excision, or the injection of sclerosing solutions. Capillary hemangiomas may be treated successfully by the application of solid carbon dioxide for 5 or 10 seconds. The treatment of large, diffuse hemangiomas is usually rather unsatisfactory. When they occur on an extremity, they may be treated as for varicose veins with ligation and the injection of a sclerosing solution. The treatment of a cirsoid aneurism should consist of extirpation of the lesion and ligation, one by one, of the afferent and efferent vessels.

The term, *hemangioendothelioma*, is applied to those blood vessel tumors that result from malignant proliferation of endothelial cells. They vary in their rate of growth, some metastasize, others do not. A special type involving bone is called Ewing's tumor.

When there is no evidence of metastasis, the treatment for hemangioendothelioma is wide surgical excision. If that is not possible, roentgen irradiation should be instituted. In general, conservative rather than radical treatment is advised. This pertains particularly to the case in which an extremity is involved, when amputation should be delayed rather than hastened. Amputation must be done, however, if the tumor cannot be controlled by surgical excision and/or high voltage roentgen therapy.

Hemangiosarcomas are usually vascular sarcomas of a high degree of malignancy which arise from fibroblastic connective tissue and vascular tissue. Relatively rare, they are characterized by rapid invasive growth, early metastasis, and a tendency to hemorrhage. Any resulting anemia should be treated by transfusions. Wide surgical excision of the tumor should be attempted, followed by roentgen irradiation. Since these tumors metastasize so early and so rapidly, treatment is usually only palliative.

Kaposi's sarcoma, usually a fatal condition, is characterized by many soft bluish nodules of the skin and by hemorrhages, the lesions are similar to infectious granulomas and under certain conditions develop neoplastic characteristics. Carefully repeated treatments with high voltage roentgen therapy is the only method found to be successful in combating the spread of the disease. It may cause involution of the lesions and prolong life, but generally it does not save life.

route Unfortunately the tetraethyl ammonium compounds are not selective in their action and unpleasant side effects often occur without much warning As the duration of the action of these drugs is approximately 2 hours they must be given by repeated daily injections The dosage must be constantly increased to secure the desired effect and this soon leads to toxic side effects and loss of any further value from the drug They are temporarily helpful when there is a severe increased spasm with pain but in general they should not be continued for more than 10 days

Dibenzylchlorethylamine (Dibenamine) gives effective prolonged blocking of adrenergic nerves and is definitely valuable in relieving vasospasm It is given in a daily dose of 5 mg per kilogram of body weight The dose should be diluted in 250 to 500 cc of normal saline or 5 per cent dextrose solution and administered intravenously The drug is to be given slowly and care must be taken to avoid extravasation *as it is irritating to tissue If a good response occurs, it is almost certain* that a sympathectomy will be successful The use of dibenzylchlorethylamine is limited to cases in which unusual vasospasm of a temporary nature has occurred or in which it is given as a temporary measure before sympathectomy It is not satisfactory for prolonged use since daily injections are usually necessary and unpleasant side effects occur not necessarily as a result of drug toxicity but as a result of the inherent property of any effective adrenergic blocking agent These reactions consist of nasal stuffiness tachycardia and occasionally a severe hypotension The recently studied drug Dibenzyline 10 to 20 mg 3 to 6 times a day is an effective oral adrenergic blocking agent which is proving to be of considerable value in the treatment of Raynaud s phenomena

Benzazoline (Priscoline) hydrochloride 25 to 50 mg 5 or 6 times a day at 4 to 5 hour intervals may give some relief The dose must be adjusted to the needs of the individual if best results are to be obtained Large doses may cause syncope and the drug should be used with care if there is a history of gastritis or gastro-intestinal ulcer The salt of the alcohol of nicotinic acid (Roniacol) tartrate in a dose of 100 to 200 mg 3 times a day may be of some help Unfortunately these drugs give only a limited amount of relief and in many patients are of no value

The pain so frequent in Raynaud s disease presents a difficult problem If it is not severe the application of an ointment containing 2 per cent nitroglycerin (Nitrol Ointment) 3 times a day will make the involved area warmer and will lessen stiffness and pain The pain may re-

CHAPTER LXV

VASOMOTOR AND TROPHIC DISTURBANCES

Raynaud's Disease

Involved extremities should be kept scrupulously clean but rubbing and the use of an irritant soap or detergent must be avoided, long soaking in water hot or cold, is also undesirable All traumas to involved parts must be avoided, including exposure to cold Burns and infections are to be guarded against, if they occur, they should receive prompt and thorough treatment Diet should be nutritious and have a high vitamin content Smoking should be interdicted Alcoholic beverages should be used only in great moderation, and should be confined to mealtime use

Periarterial sympathectomy or some form of excision of the ganglia of the chief sympathetic nerve supply to the affected extremities seems the most effective treatment for severe cases, but recurrence of symptoms is disappointingly frequent For milder cases residence in an equable climate throughout the year is advised, systematic massage and exercises involving alternate elevation and lowering of the extremities to cause at first anemia and then hyperemia of the affected part are often helpful Alternately applying and then loosening a pneumatic cuff or tourniquet is another method recommended to produce periods of anemia and hyperemia

Small doses of thyroid U S P if there is a lowered basal metabolism has sometimes helped If symptoms remain severe, a trial of drugs having a blocking effect on the sympathetic autonomic nervous system should be made Some of the following are worthy of trial

Tetraethyl ammonium bromide or chloride, given intravenously in a daily dose of 50 to 100 mg and gradually increased until the desired effect is obtained or minor toxic symptoms appear, is useful in patients showing severe temporary vasospasm A daily dose should not exceed 5 to 7 mg per kilogram of body weight if the drug is given intravenously It may be given intramuscularly in a dose of 0 5 to 1 0 gm, but 20 mg per kilogram of body weight should not be exceeded by this

instituted whenever possible, and the application of dynamic traction splints after skin softening has begun, has shown some promise

Other Trophic Diseases

For the many diseased conditions considered to belong to this group —such as erythromalalgia acrodynia erythroedema Milroy s disease or chronic hereditary edema of the legs Edgeworth s disease facial and body hemiatrophy facial and body hemihypertrophy acrocyanosis, acroparasthesia poikiloderma scleroderma adultorum ainhum lipodys trophia progressiva, and erythrocyanosis crurum puellarum frigida—there is no cure and only symptomatic therapy is of any value

BIBLIOGRAPHY

1 CONSOLE A D Diagnostic and Therapeutic Use of Tetraethyl ammonium and Dibenamine, *Am J Med* 1948 v p 164.
KLECKNER M S Jr ALLEN E V and WAKIM K G Effect of Local Application of Glyceryl Trinitrate (Nitroglycerine) in Raynaud s Disease and Raynaud s Phenomenon Studies on Blood Flow and Clinical Manifestations *Circulation*, 1951 iii p 681
3 LAGEN J B Priscoline as Adjunct for Relief of Vasospasm in Peripheral Vascular Disease *Am Pract*, 1950 i p 50
4 PRATT G H *Surgical Management of Vascular Diseases* Lea and Febiger Phila 1949
5 WRIGHT I S *Vascular Diseases in Clinical Practice* The Year Book Publishers Inc. Chicago 1948
6 ZARAFONETIS C J D Para aminobenzoic Acid in the Treatment of Scleroderma and other Disorders Associated with Excessive Fi brosis *J Mich State Med Soc* 1954, LIII 782

CHAPTER LXV

VASOMOTOR AND TROPHIC DISTURBANCES

Raynaud's Disease

Involved extremities should be kept scrupulously clean, but rubbing and the use of an irritant soap or detergent must be avoided, long soaking in water hot or cold, is also undesirable All traumas to involved parts must be avoided, including exposure to cold Burns and infections are to be guarded against, if they occur, they should receive prompt and thorough treatment Diet should be nutritious and have a high vitamin content Smoking should be interdicted Alcoholic beverages should be used only in great moderation, and should be confined to mealtime use

Periarterial sympathectomy or some form of excision of the ganglia of the chief sympathetic nerve supply to the affected extremities seems the most effective treatment for severe cases, but recurrence of symptoms is disappointingly frequent For milder cases residence in an equable climate throughout the year is advised, systematic massage and exercises, involving alternate elevation and lowering of the extremities to cause at first anemia and then hyperemia of the affected part, are often helpful Alternately applying and then loosening a pneumatic cuff or tourniquet is another method recommended to produce periods of anemia and hyperemia

Small doses of thyroid U S P if there is a lowered basal metabolism has sometimes helped If symptoms remain severe, a trial of drugs having a blocking effect on the sympathetic autonomic nervous system should be made Some of the following are worthy of trial

Tetraethyl ammonium bromide or chloride given intravenously in a daily dose of 50 to 100 mg and gradually increased until the desired effect is obtained or minor toxic symptoms appear is useful in patients showing severe temporary vasospasm A daily dose should not exceed 5 to 7 mg per kilogram of body weight if the drug is given intravenously It may be given intramuscularly in a dose of 0 5 to 1 0 gm, but 20 mg per kilogram of body weight should not be exceeded by this

PART XIX

DISEASES OF THE ENDOCRINE SYSTEM

CHAPTER LXVI

DISEASES OF THE ADRENALS

Treatment for the diseases in this category may give some of the most satisfactory results seen in medicine or prove very disappointing indeed Recent developments have made available new and valuable therapeutic agents for the treatment of diseases of the adrenals gonads and thyroid

Malfunction of the adrenals produced by a variety of conditions may *result in hyperfunction or hypofunction of the cortex or excessive* medullary action

Hyperfunction of the Adrenal Cortex

Overactivity of the type produced by a hyperactive adrenal cortex is commonly caused by hyperplasia of the adrenals or by a tumor either benign or malignant in the cortex pituitary or elsewhere Occasionally cortical hyperactivity results from hyperplasia of adrenal rests It may also result from the use of corticotropin

Cortical hyperfunction produces at least two well recognized syn *dromes depending on which hormones are elaborated in excess and the* response of the organism to them They are the adrenogenital and Cushing s syndromes

Adrenogenital Syndrome

This syndrome is usually caused by an adenoma or carcinoma of the adrenal cortex or by adrenal cortical hyperplasia Occasionally an *arrhenoblastoma or granulosa cell tumor of the ovary may be the* etiological factor Carcinoma of the cortex is the most common tumor and since metastases occur early it is necessary that diagnostic and therapeutic measures be instituted promptly as soon as the disease is suspected

quire the use of acetylsalicylic acid, 0 6 gm 3 or 4 times a day, or codeine phosphate, 30 mg 3 or 4 times a day Meperidine (Demerol) hydrochloride, 50 to 100 mg, methadone hydrochloride, 5 to 10 mg or even morphine sulfate, 8 mg, may be required for relief The narcotics should be avoided if possible

Angioneurotic Edema Quincke's Disease

If the allergenic cause can be detected, its elimination is the most effective therapeutic measure When it cannot be determined, ephedrine sulfate, 25 to 50 mg by mouth, or epinephrine (Adrenalin) hydrochloride, hypodermically, in doses of 0 3 to 0 5 cc of a 1 1000 solution should be tried, they will often bring relief If there is involvement of the throat, a spray of epinephrine hydrochloride 1 100 solution should be tried Sometimes suffocation may become imminent and will require immediate tracheotomy Corticotropin and cortisone or prednisone (Meticortin) should be tried

Diphenhydramine (Benadryl) hydrochloride, or tripelennamine (Pyribenzamine) hydrochloride, in oral doses of 50 mg 3 or 4 times a day, or the longer-acting chlorocyclizine (Perazil) hydrochloride, 50 mg by mouth once daily, may also be of value in some patients These drugs can be given in conjunction with other recommended therapy

Scleroderma

These patients must be warmly clad in winter, or must go to a warm climate, for they are especially sensitive to cold As the thyroid may be involved in the sclerotic process, thyroid extract, administered as for myxedema, is sometimes helpful The dry skin should be protected from irritation by frequent application of toilet lanolin or aquaphor ointment Only very mild soaps should be used, and soothing or oily types of lotions should be applied often to skin surfaces Corticotropin and cortisone are helpful in some patients but the unfavorable reactions occurring with long-continued use of these drugs often outweigh the favorable effects Vascular disease in early cases is occasionally relieved by the use of vasodilator drugs as recommended for Raynaud's Disease Potassium para-aminobenzoate, 12 0 gm daily given orally as a 10 per cent solution, over long periods of time (6 months to 2 years), with physiotherapy

PART XIX

DISEASES OF THE ENDOCRINE SYSTEM

CHAPTER LXVI

DISEASES OF THE ADRENALS

Treatment for the diseases in this category may give some of the most satisfactory results seen in medicine or prove very disappointing indeed Recent developments have made available new and valuable therapeutic agents for the treatment of diseases of the adrenals gonads and thyroid

Malfunction of the adrenals produced by a variety of conditions may result in hyperfunction or hypofunction of the cortex or excessive medullary action

Hyperfunction of the Adrenal Cortex

Overactivity of the type produced by a hyperactive adrenal cortex is commonly caused by hyperplasia of the adrenals or by a tumor either benign or malignant in the cortex pituitary or elsewhere Occasionally cortical hyperactivity results from hyperplasia of adrenal rests It may also result from the use of corticotropin

Cortical hyperfunction produces at least two well recognized syndromes depending on which hormones are elaborated in excess and the response of the organism to them They are the adrenogenital and Cushing s syndromes

Adrenogenital Syndrome

This syndrome is usually caused by an adenoma or carcinoma of the adrenal cortex or by adrenal cortical hyperplasia Occasionally an arrhenoblastoma or granulosa cell tumor of the ovary may be the *etiological factor* *Carcinoma of the cortex* is the most common tumor and since metastases occur early it is necessary that diagnostic and therapeutic measures be instituted promptly as soon as the disease is suspected

Operations on these patients for the removal of a tumor or resection of an hypertrophied gland is hazardous since an Addisonian crisis may develop during or subsequent to the operation A crisis is more likely to occur in patients with large tumors showing atrophy of the remaining cortical tissue Preventive measures should consist of those prescribed for the management of patients with Addison s disease who have been subjected to surgical procedures

Anatomical malformations of the genitals should be corrected by plastic surgery and embarrassing hirsuitism relieved by electrodesiccation Females are benefited by estrogenic therapy which assists in the development of secondary sex characteristics Psychotherapy is important and aids greatly in helping the patient to adjust

Cushing's Syndrome

This syndrome at first thought to be produced by basophilic adenomata of the pituitary is known now to be associated frequently with adrenal cortical hyperplasia or an adenoma or other neoplasm of the adrenal cortex ovary thymus or testis or to follow the use of corticotropin or cortisone An occasional case may be caused by hyperplasia of aberrant adrenal cortical tissue In rare cases no apparent etiological factor can be found

Once the syndrome is suspected diagnostic studies as described for adrenogenital syndrome usually reveal the causative factor

Treatment should consist of the surgical removal of the tumor or hyperplastic aberrant cortical tissue when these are the existing causes Excellent results frequently follow surgery in these cases

Patients with hyperplastic adrenals and those without any apparent endocrine abnormality present difficult therapeutic problems and are frequently benefited only moderately by therapy Partial resection of one of the hyperplastic glands may be helpful but unfortunately the improvement is usually temporary Total adrenalectomy has proved to be highly satisfactory in a few cases and with the use of cortisone and other measures recommended for Addison s Disease very little difficulty is encountered Radiation therapy to the hyperplastic adrenal is equivocal but it too when beneficial, usually gives only temporary relief

When Cushing s syndrome follows the administration of corticotropin or cortisone it gradually disappears after the use of these substances has ceased

Occasionally a tumor can be felt on palpation or is revealed by intravenous or retrograde pyelography or by x-ray following perirenal oxygen insufflation This latter procedure, although most helpful in outlining the size and contour of the adrenals, is of little value when negative It is not without hazard and should be done only by those skilled in the technique Urinary studies may show an excessive excretion of 17-ketosteroids or estrogenic hormones Fractionation of the alpha and beta isomers frequently shows an excess of beta X ray examination of the skull, bones, and lungs is indicated because of the possibility of metastases If a diagnosis cannot be made otherwise, bilateral exploration of the adrenals may be necessary The surgical approach has the additional advantage of permitting direct visualization and operative removal of a tumor or removal of a hypertrophied gland

Treatment of patients found to have an adenoma or carcinoma should consist whenever possible of surgical removal (provided there are no detectable metastases), since this offers the only hope of complete cure Successful surgical removal of a tumor usually produces most gratifying results In females there is a reversion toward the female pattern menses return breasts develop, acne disappears, the voice returns to normal libido increases and the androgen excretion decreases Hirsutism, although decreasing somewhat, unfortunately remains as a source of cosmetic embarrassment Juveniles of both sexes revert to their normal sex patterns

Patients with cortical hyperplasia as the cause of their disease are benefited, at least temporarily by surgical removal of a portion of one or both glands If necessary both of the adrenal glands can be totally removed and the patient maintained in good health by the use of cortisone desoxycorticosterone and sodium chloride as recommended for Addison's Disease Radiation therapy gives good but temporary results

Recently Wilkins has reported gratifying results using cortisone in patients with adrenal virilism caused by cortical hyperplasia When it is given in a dose of 25 mg a day for adults or 10 mg a day for children, there results a rapid suppression of excessive 17-ketosteroids in the urine within 4 or 5 days Cortisone continued over long periods of time in children causes a gradual decrease in the abnormal rates of skeletal and sexual organ growth and a restoration of normal physiological development In adults the female reverts to the feminine type menses reappear, breast tissue develops, and normal female psychology returns Unfortunately hirsuitism does not decrease The cortisone causes atrophy of the adrenal cortex

Diabetes mellitus when present, is usually mild but is resistant to insulin Control may be most difficult but management as described for Diabetes Mellitus will be satisfactory

Hypertension usually develops and may require treatment as described for Hypertension

Patients showing an excessive nitrogen loss with high serum calcium and sodium but low serum potassium should receive a diet high in protein low in sodium, and high in potassium Patients with low serum potassium are benefited by additional intake of potassium chloride or potassium citrate 10 to 16 gm daily

Individuals with high serum calcium may develop renal calculi These patients should be observed carefully and proper therapy instituted at once if a stone appears

Hypofunction of the Adrenal Cortex

Addison's Disease

Recent advances in the diagnosis and treatment of this disease are one of the most pleasing developments in modern medicine Many patients with this formerly severely incapacitating and fatal disease are now given years of comfortable useful life as a result of proper therapy Unfortunately management of patients with severe deficiencies is still complicated expensive and not entirely satisfactory but much can be done to give relief

Essentially treatment is directed toward the prevention and correction of abnormal electrolyte water and carbohydrate metabolism Perhaps in no other disease is it so imperative that active corrective measures be taken early Patients with mild degrees of deficiency may secure relief from the simplest measures when treated promptly and adequately These same patients however if neglected may become serious or even hopeless therapeutic problems

The type of therapy and mode of administration vary from one patient to another and from time to time in the same patient depending on the degree of deficiency and whether or not complicating factors are present Treatment may be divided into three general aspects management during an acute crisis regular maintenance and general supportive measures

Acute Addisonian Crisis Severe acute deficiency states with serum alterations in electrolyte water and carbohydrate metabolism may

Surgical removal of a hypersecreting tumor or resection of a portion of a hyperactive adrenal or total adrenalectomy is dangerous and unless proper pre- and post-operative measures are taken, the patient usually dies of an Addisonian crisis 2 or 3 days after the operation Accordingly, the preventive measures described for a patient with Addison's disease who is exposed to surgical procedures are recommended

Individuals without neoplasms or adrenal hyperplasia may be markedly benefited by radiation therapy to the pituitary gland Approximately one third of them receive benefit from radiation Sosman recommends 1,500 roentgens through each of 3 portals, 2 temporal and a frontal given at a rate of 300 roentgens per day for a total of 15 treatments Some of these patients show a favorable response when a daily dose of 30 mg of methyl testosterone is given orally or when 25 mg of testosterone is given intramuscularly 3 times a week The dose should be continued as long as a favorable response is apparent Unfortunately, androgen therapy accelerates the hirsutism Acne may develop and hypertension may increase Prolonged therapy with it is inadvisable Estrogens are of limited value

In view of the mental disturbances and personality changes which may be so severe as to simulate psychoses, it is important that the patients be given some understanding of their malady Such instructions will give them insight into the problems facing them and make them better able to adjust to the disease

Psychotherapy and sympathetic understanding of the patient's problems will do much to help the individual, who should be protected from emotional and physical strain and from any activity that causes fatigue Measures such as surgical correction of a hypertrophied clitoris or electrodesiccation of superfluous hair may do much to alleviate emotional tension

Infections trauma, and surgical procedures are poorly tolerated and should be avoided when possible or treated with great care and prompt measures used to avoid an Addisonian crisis Patients should be instructed to protect themselves against skin bruises which heal poorly and should be informed of the possibility of pathological fractures occurring in the decalcified weakened bones

Obesity is not desirable and careful reduction of weight is recommended The relaxed abdominal wall and pendulous breasts whether occurring in the obese or non obese patient should be corrected by the use of properly fitted supports Rapidly progressing or severe kyphosis may require a thoracic brace for relief

ously every 2 hours for the first 24 hours On the second day 25 to 50 cc is usually given in the glucose saline infusion and this is continued daily until the fever falls appetite returns and the patient is *able to take adequate nourishment by mouth and is on the way to recovery*

Desoxycorticosterone acetate 5 0 mg and cortisone 100 mg are given intramuscularly at the same time as the therapy above On the second day 25 mg of cortisone should be given every 6 hours After the first day 2 or 3 mg of desoxycorticosterone a day are usually sufficient When the patient has recovered from the acute crisis cortisone 12 5 mg 2 times a day is usually adequate

Blood pressure must be checked at 1 or 2 hour intervals during the first 24 hours and later at or 3 hour intervals until recovery is evident If the pressure falls below 90 mm mercury phenylephrine (Neosynephrine) hydrochloride 2 to 4 mg given subcutaneously 1 500 epinephrine in oil 1 0 cc given intramuscularly is also helpful Norepinephrine (Levophed) infusion as recommended above usually prevents sudden falls in blood pressure

A fall in blood pressure may mean that therapy has not been pushed vigorously enough in which case the serum sodium will be low and the hematocrit high or rising Such a fall in pressure may also mean that therapy has been pushed too vigorously and that excessive sodium and water retention is occurring In this case the hematocrit is low or falling weight increases edema may appear fever increases and drowsiness and lassitude appear Patients with the first of these two conditions should receive more vigorous therapy sodium chloride intake must be increased and the desoxycorticosterone acetate dose increased by 5 to 10 mg intramuscularly *daily Patients in the second* category should receive no more desoxycorticosterone acetate and the number of infusions and the amount of sodium chloride intake should be reduced Adrenal cortical extract dosage is to be increased to 5 or 10 cc every hour These patients receive benefit from an infusion of human albumin 25 gm or human plasma 500 cc added to a 5 per cent glucose solution Potassium deficiency may appear in these patients in sufficient degree to be serious If this occurs and the kidneys are *functioning adequately infusion of 1000 cc of a solution containing* dibasic potassium phosphate 2 0 gm monobasic potassium phosphate 0 4 gm and glucose 50 gm will hasten recovery and serve until potassium can be taken by mouth

Cardiac insufficiency with decompensation may occur when desoxy

occur suddenly, usually as the result of some strain on the organism or damage to the adrenals such as that caused by an infection, by surgical operations of any kind and especially by trauma, exposure to toxic drugs or chemicals, and surgical resection or removal of a tumor of the adrenals

Treatment must be vigorous, adequate, prompt, and directed toward the prevention or correction of shock and hypoglycemia Absolute bed rest in a quiet, pleasant room free from all noise and distraction is recommended Examination, diagnosis, and nursing procedures should be restricted to those absolutely essential for proper management If there is peripheral vascular collapse, 0 5 cc of 1 1000 epinephrine (Adrenalin) hypochloride should be given intravenously at once, followed by 4 cc of a 1 1000 solution of nor-epinephrine (Levophed) added to 1000 cc of the physiological saline solution which is permitted to flow at the rate of 20 to 30 drops per minute or as needed to maintain blood pressure at satisfactory levels A blood sample should be taken for glucose non protein nitrogen sodium, and serum protein determinations and then an intravenous infusion of 1000 cc of a solution of 10 per cent glucose in 0 85 per cent sodium chloride to which has been added 25 gm of normal human serum albumin, 2 units of plasma or 500 cc of whole blood and 50 to 100 cc of aqueous adrenal cortical extract should be given The dose of the adrenal cortical extract depends on the age of the patient and the severity of symptoms This infusion is to be repeated in 4 to 6 hours if the blood pressure remains below 80 mm of mercury The total fluid intake, however, should rarely exceed 2500 cc in 24 hours Patients who respond satisfactorily to the first infusion usually receive a second in 6 to 12 hours and a daily infusion thereafter until vomiting ceases, appetite improves, and electrolytes, glucose and temperature return to normal Morphine codeine and other narcotic analgesics and the barbiturates are contraindicated Penicillin procaine in aqueous suspension 300,000 units plus 100 000 units of soluble penicillin, every 12 hours intramuscularly, should be given until the patient is fully recovered as a preventive measure against infection or to clear up any existing infection Other antibiotics should be given in the usual dosage if needed

As time and the patient's condition permit, the causative condition should be searched for and whenever possible it should be eradicated

In conjunction with these measures hormone therapy must be pushed Aqueous adrenal cortical extract 5 cc subcutaneously, should be given promptly This should be followed in severe cases by 5 cc subcutane-

The effect of this therapy on blood pressure serum sodium weight and the general well being of the patient is to be observed for 3 to 4 days Blood sodium should be approaching normal and there should be a prompt gain in weight but this gain should not exceed 1 pound a day The appearance of edema is to be avoided Blood pressure rise is slower but usually appears after 4 or 5 days of treatment If a favorable response has not occurred by the fourth day the dose is to be increased by 0 5 mg and a further 3 day study made Usually a dose of 5 mg proves sufficient for the vast majority of patients Patients receiving cortisone 12 5 mg twice a day will usually stabilize on a dose of 0 5 to 1 0 mg of desoxycorticosterone

Once the proper dosage level is established the most desirable route of administration for the individual concerned can be decided upon Sublingual administration although convenient for the patient requires approximately 3 times the intramuscular dose and unfortunately careful dosage control is difficult This route is usually unsatisfactory for all but the mild easily regulated cases and in which there are no complications

Intramuscular or subcutaneous injections are effective easily regulated and can be given by the patient himself once he has learned the technique This route however requires daily injections and a larger dose of the hormone than pellet implantation occasionally causes local irritation and if the patient is careless local infection may develop Injection therapy is the route of choice until sufficient experience has been gained to substitute pellet implantation and for patients with severe disease difficult to regulate who are likely to have sudden fluctuation in hormone requirements

Pellet implantation is highly satisfactory for many patients It is economical affords a uniform supply of the hormone over long periods of time and simplifies the treatment for the patient The amount of hormone to be implanted depends on the intramuscular dose of desoxycorticosterone previously determined This dose is to be established by a 2 to 3 month period of observation during which time the adrenal deficiency has been maintained in a well controlled state by intramuscular injections The patient during this period is to continue normal activities and receive in addition sodium chloride 1 gm 3 *times a day after meals*

Satisfactory results are usually obtained when 1 or 2 pellets containing 125 mg of desoxycorticosterone acetate are implanted once a year Following the implantation the extra sodium chloride intake can usually be discontinued

corticosterone and sodium chloride have been pushed too vigorously If this complication appears cautious reduction in the salt and hormone intake is indicated, and the patient will be benefited by prompt digitalization and mercurial diuretics as described for cardiac decompensation

As soon as the patient's condition permits, small quantities of sweetened fruit juices, broths and carbonated beverages should be started, as improvement continues, the regular maintenance regimen is to be begun

Maintenance Therapy Sodium chloride, desoxycorticosterone, and cortisone singly or in combination, may be required for maintenance therapy The amounts needed and whether they are to be given singly or in combination depend on the severity of the deficiency and the response to management Careful clinical and laboratory evaluation is essential, since the information so gained serves as a guide to therapy

Sodium Chloride Patients with milder degrees of deficiency occasionally may be maintained in good health by only an increased intake of sodium chloride A dose of from 6 to 12 gm of sodium chloride in addition to the salt in the diet given in divided doses in the form of bouillon (the commercial cubes of which contain 2 to 2 5 gm of salt) 3 or 4 cups a day, salt dissolved in water, enteric coated pills or plain salt tablets (which however are likely to produce stomach irritation) is recommended Usually the larger dose is required for maintenance If nausea, vomiting and diarrhea are severe and interfere with treatment, or if signs of an incomplete or unsatisfactory response are present, such as failure of the blood pressure to rise to normal or weakness and fatigue treatment with desoxycorticosterone is indicated

Desoxycorticosterone Individuals not responding well to sodium chloride therapy and those with a moderate to severe degree of deficiency are benefited markedly by properly regulated desoxycorticosterone therapy This hormone exerts a powerful influence over salt and water regulation Dosage levels are to be established by careful observation in the hospital of the effects of a given dose on blood pressure sodium level of the serum and improvement of symptoms The daily maintenance dose will vary between 1 mg and 8 mg Patients receiving cortisone in a dose of 25 mg daily usually require only 0 5 to 1 0 mg Patients not receiving cortisone or sodium therapy and not in crisis or obviously rapidly approaching a crisis are to be given an initial dose of 2 to 3 mg of desoxycorticosterone acetate intramuscularly or subcutaneously once daily and 1 gm of sodium chloride, either in bouillon dissolved in water, or as an enteric coated pill after each meal

adrenal cortical extract have been added given intravenously a few hours before operation, are most beneficial Intravenous plasma 500 to 1000 cc should be given at the time of operation Injections of 10 mg of desoxycorticosterone acetate and 20 cc of adrenal cortical extract given at 6 hour intervals for 2 or 3 days are recommended Infusions of 1000 cc of 0 9 per cent sodium chloride should be repeated at 12 hour intervals when required

General management and supportive therapy are important in the treatment of hypoadrenalism The patient must be protected from stress and strain whether mental or physical Extremes of temperature are harmful and must be avoided During hot weather patients should drink more water and increase daily sodium chloride intake by 2 or 3 gm Warm protective clothing is essential in winter Trauma, surgery infection and pregnancy gastro-intestinal upsets with nausea, vomiting, and diarrhea are serious complications capable of precipitating a crisis Patients with any of these conditions must be observed carefully and corrective measures as just described taken at the first indication of difficulty Proper antibiotic therapy given early in infection may prevent serious trouble Pregnant patients with nausea and vomiting during the first trimester may require supplemental therapy only to have this need disappear as the nausea and vomiting cease and the fetal adrenals help supply the hormone needs Immediately following delivery the loss of fetal hormone is prone to precipitate a serious and often fatal crisis These patients must receive management as described for major surgery or if crisis develops the measures described for its treatment should be carried out

Patients with tuberculosis should receive the treatment recommended for its management in addition to that required for hypoadrenalism

Hemorrhage into the Adrenals Waterhouse Friderichsen Syndrome

This frequently fatal syndrome usually is caused by an overwhelming infection Most cases show extensive hemorrhage in the adrenals and some of the shock and pathological physiology observed are produced by a lack of adrenal activity

Treatment should consist of the immediate relief of shock control of infection by the proper antibiotic therapy, and the measures recom

Patients must be observed for several weeks following implantation since there may be too much or too little hormone being freed If there is insufficient hormone, sodium chloride intake should be increased and, if necessary, supplemental intramuscular injections of desoxycorticosterone acetate should be given The latter is usually unnecessary If signs of excess hormone activity appear, sodium chloride should be restricted If this measure is not sufficient, potassium citrate, 0 5 to 1 0 gm, dissolved in water and given by mouth daily, will be helpful. If severe signs of overactivity persist, it may be necessary to remove some of the implant

After several months it may be necessary to resume the increased intake of sodium chloride, especially when early signs of deficiency appear Later as the pellet becomes exhausted, intramuscular injections of desoxycorticosterone acetate should be resumed Usually an intramuscular dose of 2 to 5 mg twice weekly suffices at first, and this should be increased to daily injections as the need develops

Pellets usually supply sufficient hormone for 9 to 12 months As the pellet becomes exhausted, a careful period of observation is again necessary before a repeat implantation This observation is essential because the patient's requirements may have changed considerably during the interval since the last implant Routine implants done at the end of a year without determination of the patient's need can produce serious reactions and may be dangerous, especially in older, debilitated patients

Patients subjected to unusual stress, infections, trauma surgery, gastrointestinal upsets and with poor food intake or diarrhea are in danger of going into a crisis and consequently measures should be taken to prevent such a crisis from developing Sodium chloride intake should be increased as required and should be given by intravenous infusion if necessary Usually a dose of 3 to 6 gm will suffice

Cortisone in a dose of 12 5 mg twice a day is recommended and gives excellent results It may be given orally Occasionally 50 mg a day is necessary The dose should be increased during periods of stress Patients should have a supply of aqueous adrenal cortical extract available at all times In periods of stress such as infection, fever, and gastrointestinal upsets they should be advised to take 5 cc of the extract 2 or 3 times a day and to report at once to their physician

If major surgery is required desoxycorticosterone acetate, 10 mg cortisone 200 mg given intramuscularly and 1500 cc of 5 per cent glucose in a 0 9 per cent sodium chloride solution to which 50 cc of

BIBLIOGRAPHY

Diseases of the Adrenals

1 CAHILL G F and MONTEITH J C The Use of Dibenamine and Nor epinephrine in the Operative Treatment of Pheochromo cytoma *N E J Med* 1951 CCXLIV p 657
2 EMERSON K J Adrenal Disorders Diagnosis Pathology and Treatment *Med Clinic No Amer* September 1951 p 1283
3 ISERI L T HENDERSON H W and DERR J W Use of Adrenalytic Drug Regitine in Pheochromocytoma *Am Heart Jour* 1951 XLII p 129
4 SOSMAN M C Cushings Disease Pituitary Basophilism (Caldwell Lecture 1947) *Am J Roentgenol* 1949 LXII p 1
5 THORN G W FORSHAM P H and EMERSON K J *The Diagnosis and Treatment of Adrenal Insufficiency*, Charles C Thomas Springfield Illinois 1949

Patients must be observed for several weeks following implantation since there may be too much or too little hormone being freed. If there is insufficient hormone, sodium chloride intake should be increased and, if necessary, supplemental intramuscular injections of desoxycorticosterone acetate should be given. The latter is usually unnecessary. If signs of excess hormone activity appear, sodium chloride should be restricted. If this measure is not sufficient, potassium citrate, 0.5 to 1.0 gm. dissolved in water and given by mouth daily, will be helpful. If severe signs of overactivity persist, it may be necessary to remove some of the implant.

After several months it may be necessary to resume the increased intake of sodium chloride, especially when early signs of deficiency appear. Later, as the pellet becomes exhausted, intramuscular injections of desoxycorticosterone acetate should be resumed. Usually an intramuscular dose of 2 to 5 mg. twice weekly suffices at first, and this should be increased to daily injections as the need develops.

Pellets usually supply sufficient hormone for 9 to 12 months. As the pellet becomes exhausted, a careful period of observation is again necessary before a repeat implantation. This observation is essential because the patient's requirements may have changed considerably during the interval since the last implant. Routine implants done at the end of a year without determination of the patient's need can produce serious reactions and may be dangerous, especially in older, debilitated patients.

Patients subjected to unusual stress, infections, trauma, surgery, gastrointestinal upsets, and with poor food intake or diarrhea are in danger of going into a crisis, and consequently measures should be taken to prevent such a crisis from developing. Sodium chloride intake should be increased as required and should be given by intravenous infusion if necessary. Usually a dose of 3 to 6 gm. will suffice.

Cortisone in a dose of 12.5 mg. twice a day is recommended and gives excellent results. It may be given orally. Occasionally 50 mg. a day is necessary. The dose should be increased during periods of stress. Patients should have a supply of aqueous adrenal cortical extract available at all times. In periods of stress, such as infection, fever, and gastrointestinal upsets, they should be advised to take 5 cc. of the extract 2 or 3 times a day and to report at once to their physician.

If major surgery is required, desoxycorticosterone acetate, 10 mg., cortisone 200 mg. given intramuscularly, and 1,500 cc. of 5 per cent glucose in a 0.9 per cent sodium chloride solution to which 50 cc. of

Surgical measures are indicated if iodine therapy fails to arrest growth and enlargement is extending substernally or causes pressure on the trachea Occasionally a large goiter may present such a cosmetic handicap that it requires surgical removal If surgery is contemplated 6 to 15 mg of iodine should be given daily for 1 or 2 weeks before operation This dose is supplied by 1 cc of the syrup of hydriodic acid U S P or 1 or 2 drops of a 20 per cent solution of potassium iodide

Prevention It has been amply demonstrated that the addition of small amounts of iodine to the diet is effective in preventing these goiters The practice of adding small amounts of iodine usually 0 01 per cent potassium iodide with a stabilizer to table salt to insure widespread consumption of adequate amounts of iodine has proved an effective preventive measure If iodized salt is not used 1 teaspoonful of the syrup of hydriodic acid U S P twice a year is satisfactory The small daily dose as supplied by iodized salt is the more desirable method of administration

Adenomatous Goiter Nodular Goiter

These goiters like those of the diffuse colloid type occur frequently in endemic areas They may be simple without hyperactivity or toxic with hyperthyroidism

Adenomatous Goiter without Hyperthyroidism

Treatment for this goiter is essentially a surgical problem because of the possibility of malignant degeneration substernal growth or sudden hemorrhage into the gland producing dangerous pressure on the trachea and the tendency to develop hyperthyroidism Unless the patient can be observed closely a serious condition may exist before he is aware of any changes Because of these factors surgical removal is often recommended as a prophylactic measure

Prevention The measures recommended for the prevention of simple goiter are also effective in preventing goiter of this type However iodine should not be given after the adenomatous goiter has developed since there is a possibility that its administration at this time can cause hyperthyroidism

Adenomatous Goiter with Hyperthyroidism

Treatment for this syndrome consists of careful preparation of the

mended for Addisonian crisis If the syndrome is well established treatment is not very successful

Hyperfunction of the Adrenal Medulla Pheochromocytoma

Overactivity of the adrenal medulla leads to excess production of nor-epinephrine and epinephrine, which may be liberated continually or intermittently into the blood stream and so cause continuous or intermittent attacks of severe hypertension This overactivity is caused by a paraganglioma pheochromocytoma of the adrenal medulla. Treatment should consist of surgical removal of the neoplasm Great care must be exercised during the removal of such tumors, since manipulation often leads to an outpouring of epinephrine and severe hypertension, which may prove fatal, a sudden drop in blood pressure may follow when the tumor is removed and the level of circulating epinephrine falls The latter complication is treated by giving epinephrine (Adrenalin) hydrochloride, 1 1000 in 1 to 2 cc doses intravenously, or an infusion of nor epinephrine (Levophed), 4 cc of a 1 1000 solution in 1000 cc of physiological saline solution intravenously, as needed to maintain normal blood pressure until the condition of the patient is stabilized

Recently two methods of pre- and post-operative handling of such cases have been introduced to prevent rise in blood pressure during the operative manipulation of the tumor, and to prevent excessive fall in blood pressure after the tumor has been excised Both methods show promise but neither has been used extensively enough up to this time to determine which is the best One method, using dibenamine and nor epinephrine consists in the administration of an infusion of 500 cc of 5 per cent glucose in saline containing 5 mg of dibenamine per kilogram of the patient's body weight given over several hours beginning 24 hours before operation During operation an infusion of 0 cc nor epinephrine (Levophed), 1 1000 in 500 cc saline is given slowly, to be repeated over a 36-hour period if blood pressure begins to decline significantly The other method, using Regitine and nor-epinephine, consists of the administration of -5 mg Regitine orally and 3 0 mg intramuscularly just before operation If a rise in blood pressure occurs during operation, single injections of 5 0 mg Regitine should be given intravenously If a post-operative fall in blood pressure occurs an infusion of nor-epinephrine (Levophed), 1 1000, 2 0 cc 500 cc saline, should be given slowly intravenously and repeated for 36 hours post-operatively as necessary

Medical Treatment Patients selected for medical treatment are to be advised carefully about the cyclic nature of their disease the type of treatment to be employed, and the necessity for repeated observation and evaluation They are to be warned at the outset of the possibility of recurrence following cessation of therapy The various agents now available are iodine propylthiouracil methyl mercaptoimidazole (Tapazol) x ray and radioactive iodine

Iodine can be useful in treating patients with mild very early, primary hyperthyroidism when there is little or no hypertrophy of the gland *The maximum response is obtained with a dose of 6 to 15 mg* of iodine daily This is supplied by 1 cc of the syrup of hydriodic acid U S P or 1 or 2 drops of a 20 per cent potassium iodide solution given daily The chosen drug should be continued for at least 6 months after the basal metabolism falls to normal Response to therapy should be checked by basal metabolism tests repeated at monthly intervals for the first 3 months and then at 3 month intervals for 6 months and finally at 6 month intervals for 1 year The metabolism should fall promptly to, and remain normal If it fails to do so or rises again after iodine is discontinued, or if a drug reaction to iodine develops the use of propylthiouracil is recommended

Iodides should *not be given to* patients known to be sensitive to them or to patients with tuberculosis Individuals with moderate to severe *hyperthyroidism and those with enlarged glands are better treated with* propylthiouracil along with iodides given as supplemental therapy Since the antithyroid drugs and radioactive iodine have been in use iodine alone is generally no longer given

Propylthiouracil is the medical agent of choice for the majority of patients It is the least toxic of the highly effective agents and, when combined with the iodides is the most satisfactory substance available for the medical treatment of thyrotoxicosis

Treatment consists of administering 50 to 100 mg doses of propyl thiouracil at 6 to 8 hour intervals until a total daily dose of 0 3 to 0 6 gm has been given It is recommended that the dosage be arranged to insure constant drug activity during the entire 24 hour period It is seldom necessary to exceed 0 4 gm a day The drug in full dosage is to be continued until all signs and symptoms of the disease have been brought under control and the basal metabolism is normal or slightly below normal *The required dosage may change considerably during* the course of treatment and consequently patients must be checked to avoid hypothyroidism

CHAPTER LXVII

DISEASES OF THE THYROID

The thyroid gland is subject to, and produces a variety of, diseased conditions The most important of these are simple goiter (diffuse colloid goiter), adenomatous goiter or nodular goiter with or without hyperactivity exophthalmic goiter (Grave's disease), myxedema (Gull's disease), cretinism, thyroiditis, and malignant degeneration

Simple Goiter Diffuse Colloid Goiter

The endemic simple goiter consisting of a uniformly enlarged thyroid gland usually appears at puberty or during pregnancy Since the introduction of iodized salt, the incidence of this condition has fallen markedly If it is noticed *early in pregnancy or in young children*, the prompt administration of 2 to 4 mg of iodine weekly for several months will usually prevent further development and occasionally the goiter will disappear or decrease in size This dosage is supplied by 5 to 10 drops of the syrup of hydriodic acid U S P or 1 drop of 20 per cent potassium iodide solution The strong solution of iodine U S P [Lugol's solution] is unpleasant to the taste, but may be used The commonly prescribed saturated solution of potassium iodide varies in iodide content administered, since its solubility changes with temperature A 20 per cent solution has a stable iodide content and 1 drop gives approximately 10 mg of iodine The patient should be maintained on iodized salt

After the goiter is well developed, iodine therapy usually causes no atrophy but is capable of arresting further growth Iodine therapy is of no value for adult patients who have had a goiter for years and there is a possibility that it may be harmful to such individuals if given in large doses

If metabolism is lowered and there are signs of hypofunction, desiccated thyroid U S P 60 mg 2 times a day, should be given and this dose increased or decreased as indicated by basal metabolic studies

Medical Treatment Patients selected for medical treatment are to be advised carefully about the cyclic nature of their disease, the type of treatment to be employed, and the necessity for repeated observation and evaluation They are to be warned at the outset of the possibility of recurrence following cessation of therapy The various agents now available are iodine propylthiouracil methyl mercaptoimidazole (Tapazol), x ray and radioactive iodine

Iodine can be useful in treating patients with mild very early, primary hyperthyroidism when there is little or no hypertrophy of the gland The maximum response is obtained with a dose of 6 to 15 mg of iodine daily This is supplied by 1 cc of the syrup of hydriodic acid U S P or 1 or 2 drops of a 20 per cent potassium iodide solution given daily The chosen drug should be continued for at least 6 months after the basal metabolism falls to normal Response to therapy should be checked by basal metabolism tests repeated at monthly intervals for the first 3 months and then at 3 month intervals for 6 months and finally at 6 month intervals for 1 year The metabolism should fall promptly to, and remain normal It it fails to do so or rises again after iodine is discontinued or if a drug reaction to iodine develops the use of propylthiouracil is recommended

Iodides should not be given to patients known to be sensitive to them or to patients with tuberculosis Individuals with moderate to severe hyperthyroidism and those with enlarged glands are better treated with propylthiouracil along with iodides given as supplemental therapy Since the antithyroid drugs and radioactive iodine have been in use iodine alone is generally no longer given

Propylthiouracil is the medical agent of choice for the majority of patients It is the least toxic of the highly effective agents and when combined with the iodides is the most satisfactory substance available for the medical treatment of thyrotoxicosis

Treatment consists of administering 50 to 100 mg doses of propylthiouracil at 6 to 8 hour intervals until a total daily dose of 0 3 to 0 6 gm has been given It is recommended that the dosage be arranged to insure constant drug activity during the entire 24 hour period It is seldom necessary to exceed 0 4 gm a day The drug in full dosage is to be continued until all signs and symptoms of the disease have been brought under control and the basal metabolism is normal or slightly below normal The required dosage may change considerably during the course of treatment and consequently patients must be checked to avoid hypothyroidism

patient and then surgical removal of the goiter The preparatory measures are the same as those advised for the surgical treatment of exophthalmic goiter

If severe heart damage has occurred, or if there are other complicating factors prohibiting operation, medical treatment as recommended for exophthalmic goiter is advisable Patients receiving medical treatment must remain under close observation, since malignant degeneration growth with pressure on the trachea, or hemorrhage into the gland may occur

Exophthalmic Goiter (Grave's, Basedow's or Parry's Disease) Hyperthyroidism

Recent developments in the therapy of this syndrome have made new and valuable agents available for its treatment Selection of the proper agents and plan of therapy is essential to successful management

Treatment may be solely medical or may be medical followed by surgery In general medical therapy alone is recommended for children adolescents, aged persons, and patients during pregnancy, or those with milder degrees of hyperthyroidism whose glands are not enlarged or show only slight diffuse enlargement It is also indicated for patients with recurrent hyperthyroidism showing relapse after subtotal thyroidectomy and those with serious heart disease, exophthalmos, or other complicating conditions prohibiting surgery Excellent results can be secured from medical treatment alone if the patient is properly selected The best cases for medical treatment are young patients with mild to moderate hyperthyroidism showing no enlargement or only slight diffuse enlargement of the gland

Medical treatment immediately followed by surgery is recommended for patients with large, growing, nodular, or substernal goiters, those with severe degrees of hyperthyroidism, recurrent hyperthyroidism following medical treatment acromegalic thyrotoxicosis, and patients developing drug sensitivity or those unable to be observed properly

Pre-operative preparation followed by subtotal thyroidectomy is still the procedure of choice for the majority of thyrotoxic patients It has a higher mortality than medical treatment however, completely incapacitates the patient for a longer period of time may be more expensive and there is always the possibility of hypoparathyroidism, laryngeal palsy, severe exophthalmos, and myxedema developing after operation

early reports indicate that it is fully as efficient as propylthiouracil in the management of hyperthyroidism

X ray therapy in a dose of 1000 to 2000 roentgens repeated every 3 to 12 weeks may be of value in controlling hyperthyroidism Some claim good results A gland made hyperplastic by propylthiouracil may possibly be more sensitive to x ray therapy Usually remission requires 8 to 12 months and there is likely to be skin destruction and transient esophagitis and tracheitis X ray therapy should be given only if surgery is not possible or if the patient has failed to remain in remission on antithyroid drug therapy or if radioactive iodine is not available

Radioactive Iodine The treatment of thyrotoxicosis with radioactive iodine, I 130, I 131, *and more recently with the introduction of I 132* is becoming rapidly the treatment of choice and is replacing other methods At first considered advisable for use principally in older patients in those who refused surgery, or those who have not responded satisfactorily to propylthiouracil radioactive iodine is now administered more routinely to all cases of hyperthyroidism Two disadvantages at present are lack of universal availability and the requirement of special personnel to use it

Treatment must be given by trained personnel and special precautions must be taken to protect these people from radioactivity The dose varies from 2 to 36 millicuries It is calculated by a special formula and takes into consideration the amount of thyroid tissue present Usually a dose of 0 05 to 0 15 millicuries per gm of thyroid tissue is sufficient Results from this therapy are good The patients like it and there is no danger of parathyroid deficiency laryngeal paralysis or drug reaction It is less expensive than surgery patients are ambulatory and as yet the only complication that has appeared is myxedema and this may have been due to inaccurate calculation of dosage Insufficient time has elapsed to judge whether there will be more serious postradiation effects To date, there no indications of any such complicating factors

Medical Treatment Followed by Surgery Patients selected for this treatment should be started immediately on propylthiouracil in the same dose and manner as described under medical treatment When the basal metabolism has fallen to 15 or 20 per cent iodine as 1 cc of the syrup of hydriodic acid U S P or 1 or 2 drops of a 20 per cent solution of potassium iodide should be given daily Subtotal thyroidectomy should be performed as soon as all signs of hyperthyroid activity have disappeared, the basal metabolism is normal and the thyroid is filled with colloid

patient and then surgical removal of the goiter The preparatory measures are the same as those advised for the surgical treatment of exophthalmic goiter

If severe heart damage has occurred, or if there are other complicating factors prohibiting operation, medical treatment as recommended for exophthalmic goiter is advisable Patients receiving medical treatment must remain under close observation, since malignant degeneration growth with pressure on the trachea, or hemorrhage into the gland may occur

Exophthalmic Goiter (Grave's Basedow's or Parry's Disease) Hyperthyroidism

Recent developments in the therapy of this syndrome have made new and valuable agents available for its treatment Selection of the proper agents and plan of therapy is essential to successful management

Treatment may be solely medical or may be medical followed by surgery In general, medical therapy alone is recommended for children, adolescents, aged persons, and patients during pregnancy, or those with milder degrees of hyperthyroidism whose glands are not enlarged or show only slight diffuse enlargement It is also indicated for patients with recurrent hyperthyroidism showing relapse after subtotal thyroidectomy and those with serious heart disease exophthalmos, or other complicating conditions prohibiting surgery Excellent results can be secured from medical treatment alone if the patient is properly selected The best cases for medical treatment are young patients with mild to moderate hyperthyroidism showing no enlargement or only slight diffuse enlargement of the gland

Medical treatment immediately followed by surgery is recommended for patients with large growing, nodular, or substernal goiters those with severe degrees of hyperthyroidism, recurrent hyperthyroidism following medical treatment acromegalic thyrotoxicosis, and patients developing drug sensitivity or those unable to be observed properly

Pre operative preparation followed by subtotal thyroidectomy is still the procedure of choice for the majority of thyrotoxic patients It has a higher mortality than medical treatment however, completely incapacitates the patient for a longer period of time, may be more expensive and there is always the possibility of hypoparathyroidism, laryngeal palsy severe exophthalmos, and myxedema developing after operation

glucose solution containing 1 0 gm sodium iodide is recommended These patients should receive adequate sedation with phenobarbital 0 1 to 0 3 gm which may be given intravenously if convulsions occur In case of severe excitement the dose may be repeated in 4 to 6 hours Oxygen inhalation is helpful All noise excitement movement and manipulation must be kept to the minimum Calm reassurance and psychotherapy accomplish much for these patients

Cardiac complications such as auricular fibrillation and decompensation should be treated as soon as the thyrotoxicosis is controlled They do not respond well to treatment during hyperthyroidism

Occasionally hypothyroidism occurs after surgery In these cases it should be treated as described in the following section

Hypothyroidism

Hypothyroidism resulting from abnormalities of the thyroid or pituitary glands produces cretinism if it occurs in infancy and childhood and myxedema when it occurs in juveniles or adults

Cretinism

Successful treatment of cretinism depends on its early recognition and prompt institution of adequate thyroid therapy The dose must be adjusted to the needs of the individual child and will vary with growth and development The initial dose should be small and should be increased gradually to the optimum amount needed for normal development Thyroid therapy must be continuous and the dose pushed to near toxic levels if maximum benefit is to be secured The following schedule is useful as a guide

Age of Patient	*Daily Dose*
to 4 months	6 0 mg
4 to 8 months	12 to 15 mg
8 to 12 months	15 to 20 mg
1 to 4 years	60 to 90 mg
4 to 12 years	90 to 180 mg

If the dose is too small both mental and physical development will lag In general dosage increases should not be made more often than at 1- or 2 month intervals and the dosage increment should not exceed 15 to 30 mg

The basal metabolic rate should fall approximately 1 per cent a day with adequate therapy When it has reached normal or preferably slightly subnormal values, maintenance therapy consisting of 50 to 100 mg of propylthiouracil a day should be begun The exact amount required for adequate maintenance of the individual patient is established by repeated basal metabolic rate determinations It may vary from 50 mg a day to 50 mg 2 times a week or less Maintenance therapy should be continued for 6 months After administration of the drug has been stopped the patient should be seen at 1- or 2-month intervals for 6 months and then at 3-month intervals for 1 year If hyperactivity returns the treatment is to be repeated and the maintenance dose continued for a year If there is another relapse, cessation of propylthiouracil followed by surgery is recommended Approximately 50 per cent of patients will remain in remission after the first course and 80 per cent after a second course

The patient receiving propylthiouracil must be cautioned to report immediately any untoward development such as coryza, sore throat fever, skin rash lassitude arthralgia, nausea, or any other suspicious sign or symptom In the beginning white blood cell counts should be taken and differential smears made at weekly intervals for 1 month Later these studies may be made at monthly intervals or at the first appearance of any possible indication of toxicity The drug should be discontinued if fever or definite blood changes appear Patients with mild skin rashes may tolerate the drug in a reduced dose Since the drug appears in the milk of nursing mothers it should be discontinued in such individuals or formula feedings should be prescribed for the infant The drug is not recommended during pregnancy, since it is capable of causing harm to the foetus

Iodine assists the antithyroid effect and reduces the hyperplastic changes produced by propylthiouracil It can be started as the basal metabolism approaches normal and should be continued for at least 3 months after propylthiouracil has been discontinued A dose of 1 cc of the syrup of hydriodic acid U S P or 1 or 2 drops of a 10 per cent solution of potassium iodide daily is recommended

Methylthiouracil given in the same dosage and manner may be substituted for propylthiouracil if desired It has no advantages over the propyl derivative, however

Methyl-mercaptoimidazole (Tapazol) is also effective Its dosage is approximately one twenty-fifth that recommended for propylthiouracil Experience with methyl mercaptoimidazole is not extensive as yet but

earlier phase of treatment so that they can be observed closely and the dosage adjusted as indicated by the response of the patient

Thyroid U S P is the drug of choice and the dosages given here apply to its use only Some of the other available preparations are made with a different potency and consequently they cannot be substituted in equivalent dosage for thyroid U S P If one of these is selected for use it must be employed throughout treatment since the difficulties produced by varying potency in the different preparations should be avoided Treatment may be pushed more vigorously in younger patients without any complicating diseases For these patients an initial dose of 60 to 100 mg daily by mouth rapidly increased to 100 to 200 mg daily is satisfactory This dosage is to be continued for 10 days unless untoward signs such as muscle cramps angina pectoris or cardiac failure develop Then it should be reduced to 60 to 100 mg daily If complications develop the drug should be discontinued for 4 to 5 days and then recommenced with a dose of 30 to 60 mg If severe complications develop the treatment described for patients with complicated myxedema is recommended

A daily maintenance dose of thyroid U S P 100 mg is satisfactory for the majority of these patients but individual adjustments must be made Those individuals whose metabolism has not risen to normal and who still have clinical signs and symptoms of myxedema should receive more thyroid The maintenance dose should be increased to 120 mg, and if after 2 to 3 weeks relief has not been secured the dose may be increased to 200 mg Since the drug is cumulative dosage increase must be gradual so that the maximum effect of the previous dosage can be evaluated properly Usually 2 or 3 weeks is adequate time to allow for the determination of the results of a dosage increment

Extreme caution should be used in prescribing any sedatives particularly morphine and the barbiturates to patients with myxedema

Pituitary Myxedema

Treatment for myxedema resulting from pituitary hypofunction requires thyroid therapy for control of the hypothyroidism and management of the associated hypogonadism and adrenocortical hypofunction Thyroid must be given cautiously since relief of hypothyroidism increases adrenocortical failure

Thyroid U S P 15 mg by mouth daily gradually increased to 45 to 60 mg daily as the patient s tolerance permits is recommended for these

If desired, or if the patient cannot be properly checked or is sensitive to propylthiouracil, iodine may be given alone with good effect Patients receiving iodine alone usually require from 2 to 3 weeks before they are adequately prepared for operation

Supportive Measures Patients with thyrotoxicosis must receive abundant mental and physical rest, and their activities should be curtailed until the disease is brought under control Bed rest is essential if the toxicity is severe or if there is any cardiac impairment Tense, hyperactive, emotionally unstable patients and those who cannot sleep or relax properly are benefited by phenobarbital, 15 mg by mouth 4 times a day

A well-balanced diet—palatable and high in protein, carbohydrate minerals, and vitamins—is recommended Alcohol, coffee, and tobacco should be eliminated or their intake greatly curtailed If the disease has been of long standing, and there is severe calcium loss, calcium gluconate or calcium lactate, 3 gms by mouth daily in divided doses is recommended If evidence of vitamin deficiency is present multi vitamin tablets (Multicebrin), 3 times a day, are recommended If vitamin B_1 deficiency is present, thiamine chloride in 10 mg doses should be given by mouth 2 or 3 times a day Some advocate the routine use of thiamine chloride in the treatment of hyperthyroidism

Treatment of Complications Exophthalmos, when marked, presents a serious problem and one most resistant to therapy Since the removal of thyroid tissue accelerates the process, subtotal thyroidectomy should be avoided Medical treatment with iodine and desiccated thyroid alone or combined with irradiation of the pituitary and posterior parts of the orbit is helpful Desiccated thyroid given to the limit of tolerance seems to afford the most relief

Hypothyroidism must be avoided and if present, its relief by appropriate doses of desiccated thyroid produces definite improvement in the exophthalmos

Application of pads of sponge rubber to the eyes at night may prevent some of the swelling that occurs at this time

Severe progressive exophthalmos may require surgical decompression of the bony orbit in order to prevent blindness Surgery should be reserved for the grave cases since in general it is not satisfactory Enucleation is required if panophthalmitis develops

Thyroid crisis can be prevented in almost every instance by prompt and proper management of severe cases When it does occur, the immediate intravenous administration of 1000 cc of 5 or 10 per cent

tain etiology Chronic thyroiditis exists in two well recognized forms, the lymphoid struma of Hashimoto and the fibroid struma of Riedel

Acute Thyroiditis

Acute thyroiditis resulting from infection and inflammation of the thyroid gland requires prompt and vigorous treatment Bed rest is nec essary during the acute phase Specific therapy with the antibiotic most effective against the invading organism should be initiated immediately Penicillin or aureomycin is usually most effective in these infections Sufficient fluid is given to insure a daily urinary output of 2000 cc

Local swelling and discomfort are lessened by the application of an ice bag Analgesics may be required for relief of pain and restlessness. Usually acetylsalicylic acid 0 6 gm by mouth 3 or 4 times a day is sufficient and in some cases this gives complete relief followed by prompt recovery from the inflammation Phenobarbital, 30 mg orally 3 times a day given with the acetylsalicylic acid is recommended if the latter alone proves insufficient Occasionally codeine phosphate 30 to 60 mg daily by mouth is required to afford satisfactory relief

Roentgen irradiation frequently gives excellent results Treatment must be administered by one skilled in the technique if best results are to be obtained

Propylthiouracil 0 1 to 0 2 gm by mouth 3 times a day for 1 week, followed by 0 2 gm by mouth once a day for 2 weeks may be helpful and warrants trial

Patients must be observed closely and if suppuration or signs of pressure on the trachea or esophagus appear prompt surgical intervention is essential

Since myxedema may follow a severe thyroiditis sometimes even a mild one these patients should be observed for several months after recovery

Lymphoid Struma (Hashimoto)

If the diagnosis of thyroiditis of the struma lymphomatosa type is made before operation a trial period of roentgen irradiation should be given Usually however the true nature of this thyroiditis is not recognized until surgery has been undertaken If recognized at operation, conservative resection of both lobes is recommended

Fibrous Struma (Riedel)

Treatment should consist of rest sedation and surgical removal of

Overdosage in children may produce fever, tachycardia, nausea, vomiting, overactivity, and irritability. Cardiac pain, cramps in the muscles of the extremeties, and heart failure occasionally occur with excessive overdosage.

Cretins are exceedingly prone to develop infections that often prove fatal. Therefore, they must be protected from exposure to intercurrent infections and the slightest infection must receive prompt, vigorous therapy. Protective immunization should be done whenever possible. Adenoid and tonsil tissue must be removed if it becomes the source of infection since middle-ear and mastoid involvements are likely to occur in these children. They should be protected against cold, overexertion and unusual mental and physical strain.

Untreated, long-standing cretinism in older children and endemic cretinism are not generally benefited by thyroid therapy. Occasionally this form of treatment makes the patient restless, irritable, and unmanageable without producing any improvement in the mental and physical state.

Excessively large goiters and those producing respiratory difficulty or pressure on the esophagus should be removed.

Prevention. Endemic cretinism is controlled by the measures taken to eliminate endemic goiter.

Juvenile Myxedema

Treatment for juvenile myxedema is the same as that described for cretinism. Care must be taken to avoid too rapid increase in thyroid dosage since these children are prone to develop psychoses. Basal metabolism should be brought to normal. If growth and mental development lag, thyroid medication should be pushed cautiously until the basal metabolism is maintained slightly above normal.

Myxedema. Gull's Disease

The response of this disease to thyroid medication is one of the most pleasing observations in medicine. A cold, listless, sluggish, uninteresting, seemingly dull individual under treatment is gradually converted into a normal, lively, responsive, and intelligent person.

Thyroid by mouth, given in the smallest dose required to produce a complete remission of all signs and symptoms of the disease, is recommended. The dosage employed initially and subsequently must be determined for each individual. Patients should be hospitalized during the

CHAPTER LXVIII

DISEASES OF THE THYMUS AND THE PARATHYROID GLANDS

Modern opinion favors the view that the thymus is seldom the cause of tracheal obstruction and as a consequence treatment of what appears to be an enlarged thymus gland is now of little importance If it is determined by careful study that the thymus is causing obstruction cautious roentgen irradiation by a skilled therapist affords excellent results

Tumors of the thymus and especially those producing tracheal obstruction should be removed surgically Myasthenia gravis is occasionally markedly ameliorated by the removal of an associated thymic tumor

The parathyroid glands may be involved by tumors cysts hemorrhage infection and trauma They may be removed surgically or undergo hypoplasia or hyperplasia with the result that there occurs either hypofunction causing tetany or hyperfunction leading to hyperparathyroidism generalized osteitis fibrosa cystica and renal calculi

Tetany

Tetany caused by hypoparathyroidism gives the same clinical findings and the treatment for it is similar to that used in the treatment of tetany caused by various other conditions Therapeutic management consists of measures taken to control the acute attack those required for maintenance of freedom from attack and treatment of the underlying disease

Acute tetany with muscle spasm and cramps is relieved promptly by the slow intravenous injection of 10 cc of a 10 per cent solution of calcium gluconate Injections may be repeated as needed to secure relief Calcium chloride 5 to 10 cc of a 10 per cent solution given slowly intravenously is effective also Calcium chloride is highly irritating to tissue and care must be taken to avoid getting any of the solution outside the vein Care must be taken also in giving intravenous calcium to

patients Patients developing tachycardia, excessive sweating, and an elevated basal metabolism are receiving too much thyroid, and the maintenance dose must be reduced

The most satisfactory maintenance dose is the smallest amount of thyroid that completely removes all signs and symptoms of myxedema. Careful observation over a period of time is required to establish the proper maintenance dose The basal metabolism, although of great importance, should not be the sole criterion on which therapy is based If complete symptomatic relief is secured by a given dose of thyroid, that dose may be considered adequate even though the basal metabolism may not be entirely normal Myxedematous patients with complicating diseases such as arteriosclerosis, angina pectoris, and congestive heart failure must be treated cautiously The initial dose of thyroid must not be over 15 mg daily If this is well tolerated, the dose may be increased by 15 mg after 4 weeks Usually a dose of 30 to 45 mg is tolerated by these patients At times they present most difficult problems in regulation The difference between comfort and distress may depend on a change in thyroid dosage of as little as 5 mg

As the complicating disease improves, usually more thyroid can be tolerated Patients with angina pectoris and anemia become much more tolerant to thyroid as soon as the anemia is corrected

Patients with diabetes mellitus and myxedema or those who develop apparent diabetes as the myxedema is relieved by thyroid do better on somewhat smaller maintenance doses A dose of thyroid U S P 45 to 60 mg daily is usually satisfactory Larger doses are occasionally tolerated but care must be taken to avoid increasing the severity of the diabetes mellitus

Psychoses caused by myxedema are usually benefited by treatment with thyroid but psychoses appearing during treatment require cautious handling with the administration of thyroid as described for patients with angina pectoris or cardiac decompensation

Once the maintenance dose is established, it should be continued indefinitely Patients must be instructed about the importance of continuous therapy and the necessity of periodic examinations to determine the status of the disease

Thyroiditis

Thyroiditis may occur in an acute or chronic form The acute variety is apparently of infectious origin while the chronic types are of uncer

A dose of 30 cc of aluminum hydroxide gel (Amphojel) or even better, basic aluminum carbonate gel (Basaljel) in the same dose by mouth 3 or 4 times a day is effective

These patients must be observed closely for long periods of time since changes in calcium requirements are likely to occur

Hyperparathyroidism

Treatment consists of preparing the patient for surgical removal of the tumor or hypertrophied parathyroid tissue Before operation patients should be hospitalized receive bed rest and be placed on a low-calcium low phosphorus diet Milk cheese and eggs should be omitted Sufficient fluid intake to maintain an output of 000 to 2500 cc of urine daily is recommended and the urine should be made acid in reaction *High serum phosphorus may be lowered by aluminum hydroxide gel (Amphojel) or basic aluminum carbonate gel (Basaljel) 30 cc by* mouth 3 times daily If there is a renal stone with severe infection this should be removed and the infection cleared before parathyroidectomy

If an adenoma is present it should be excised completely Nearly all hypertrophied parathyroid tissue should be removed Only one of the glands should be left and depending upon the degree of hypertrophy only a portion of it should remain If the blood serum phosphorus is elevated more parathyroid tissue should be left

If tetany develops post operatively treatment as recommended for *hypoparathyroidism is recommended*

Patients with osteitis fibrosa may develop severe tetany post operatively requiring intravenous calcium gluconate in repeated doses for relief These patients must be protected from and warned about the danger of fractures until bone has recalcified

BIBLIOGRAPHY

Diseases of the Thymus and the Parathyroid Glands

1 ALBRIGHT F and REIFENSTEIN E C Jr *The Parathyroid Glands and Metabolic Bone Disease* Williams and Wilkins Company Baltimore 1948
2 BARR D P Diseases of the Parathyroid Gland *Oxford Medicine,* Vol III Part III Chapter XV p 829
3 SEYBOLD W D McDONALD J R CLAGETT O T and GOOD C A Tumors of the Thymus *J of Thoracic Surgery* 1950 XX p 195

the degenerating adenoma if symptoms of pressure appear Care must be exercised to save as much of the gland as possible Skillful dissection may enable the surgeon to remove the adenomatous mass without much destruction or removal of non-involved thyroid tissue

Roentgen irradiation is of little or no value and can prove harmful when it destroys normal thyroid tissue

Myxedema may appear following surgical or x-ray treatment

Tumors

Abnormal enlargement of the thyroid gland may be produced by actinomycosis, parasitic diseases, syphilis, tuberculosis, and malignancy

Treatment for tumors of infectious etiology consists of applying those measures for control that are described for the particular disease and correction of any abnormal thyroid function

Malignant tumors should be treated surgically followed by thorough irradiation by x-ray or radium Radioactive iodine is helpful in patients with recurrence, metastatic, or unoperable malignancy Treatment must be given by those skilled in the technique If the tumor shows a good iodine response to a tracer dose, the immediate results are usually excellent in that the tumor masses disappear, and the patient appears and feels normal

BIBLIOGRAPHY

Diseases of the Thyroid

1 BURROWS B A, and ROSS, J F "The Management of Hyperthyroidism' *Med Clinic No Amer*, September 1951, p 1305
2 COPE O "Medical Progress Diseases of the Thyroid,' *N E J Med*, 1952 CCXLVI, pp 368 408 451
3 CHAPMAN, E A, and MALOOF F "The Use of Radioactive Iodine in the Diagnosis and Treatment of Hyperthyroidism Ten Years' Experience *Medicine*, 1955, XXXIV, 261
4 MEANS J H *The Thyroid and Its Diseases*, J B Lippincott Company, Philadelphia, second edition, 1948
5 REVENO W S and ROSENBAUM, H "Treatment of Acute Thyroiditis with Antithyroid Drugs,' *N E J Med*, 1951, CCXLV, p 364
6 STANLEY M M and ASTWOOD E B Notes and Comments 1 methyl 2 mercaptoimidazole an Antithyroid Compound Highly Active in Man' *Endocrinology*, 1949, XLIV, p 588
7 WAHLBERG J 'Thiouracil Treatment and Its Indications," *Acta Med Scandinav*, 1949 CXXXII p 431

Acromegalic patients with less serious damage who have local pressure symptoms without acute rapidly progressing eye impairment, are best treated by x ray

Roentgen irradiation is effective and when it is given early in adequate dosage, the results are usually good Irradiation should be given by a roentgenologist skilled in the technique, and he should determine the dosage and method of administration In adults a total dose of less than 6000 roentgens is essential if brain damage is to be avoided, in children, a total dose of 3000 to 4500 roentgens should not be exceeded Improvement following x ray therapy is gradual and 1 to 2 months may be required for proper evaluation Immediately after therapy, eye impairment may temporarily grow worse, probably as a result of the edema and reaction produced locally by irradiation

Usually headaches disappear visual fields improve, and if dosage has been sufficient, some depression of endocrine hyperactivity will result

Patients must be observed closely by repeated follow up examinations and further treatment given when it is apparent that the disease is again progressing

Acromegalic patients who do not respond to x ray therapy probably have a radiation resistant tumor and will require surgical intervention for relief

Abnormal endocrine functions resulting from pituitary hyperactivity may be mild and require little or no therapy after radiation has decreased pituitary hyperfunction or may be sufficiently severe to require measures directed toward their relief

Diabetes mellitus occurring in these patients should be treated with diet and insulin as described for the control of Diabetes Mellitus Generally this form of diabetes mellitus is difficult to control, and at times its management taxes the skill of the physician and the patience of the patient.

If polyuria without glycosuria is present pituitrin used as described for Diabetes insipidus is recommended

Female patients showing signs of sex hormone lack are frequently benefited by diethylstilbestrol, 0 5 to 1 0 mg by mouth daily Patients receiving sex hormone therapy should be watched carefully, and periods of a week should be given every month or two during which time the hormone is withheld

If nausea and vomiting appear the drug should be given at bedtime Chlorpromazine (Thorazine) 25 to 50 mg by mouth 3 or 4 times a

patients who are taking digitalis, since cardiac deaths can occur from the use of these two drugs simultaneously

Once the acute muscle spasm is relieved treatment should consist of measures directed toward maintaining a normal calcium level Calcium chloride as a 25 per cent solution in syrup given by mouth in a dose of 2 gm 4 times a day is highly effective and not unpleasant to take Calcium gluconate powder, 5 gm 3 times a day, or calcium lactate powder 4 gm 3 times a day, may be substituted for calcium chloride in less severe cases they are more palatable but less effective than the calcium chloride Dilute hydrochloric acid, 10 cc taken immediately following calcium gluconate or calcium lactate, enhances the calcium absorption

Dihydrotachysterol (A T 10) (Hytakerol), 2 5 to 5 mg is to be given by mouth until the tetany is relieved The dose is then to be reduced to 1 25 to 2 5 mg once or twice a week for maintenance

Once the acute phase is over and the calcium phosphorus ratio remains normal with small maintenance doses of dihydrotachysterol, it may be replaced by the less expensive vitamin D [calciferol U S P] The dose of vitamin D [calciferol] required varies with the patient from 400,000 U S P units daily to 50 000 U S P units 3 times a week or less

Blood calcium and phosphorus levels should be followed closely, and the Sulkowitch test done daily until the patient s condition has become well stabilized The Sulkowitch test serves as a useful guide to therapy If the urine remains clear after thorough mixing with an equal amount of the reagent, there is no calcium in the urine this indicates a serum calcium of 5 to 7 5 mg per 100 cc If a fine cloud appears, the serum calcium is normal If a milky white cloud appears, the serum calcium level is elevated The dosage of dihydrotachysterol and vitamin D may be regulated up or down by these daily findings

Parathyroid extract, although helpful, is slower acting and less effective than dihydrotachysterol It is not recommended in the treatment of acute tetany, and since tolerance to it develops rather rapidly, it soon becomes ineffective and consequently has limited value for maintenance therapy

Blood serum proteins should be checked and if they are found to be abnormally low 50 gm of serum albumin when available, or 1 to 2 units of plasma should be given daily until normal values are secured

The diet should be high in calcium and low in phosphorus Milk, because of its high phosphorus content, should be omitted The serum phosphorus level may be kept down by the removal of phosphorus from the bowel through the absorptive action of aluminum hydroxide

of the pituitary tumors in adjacent structures and (rarely) by infection

Treatment should be directed toward relief of the intracranial lesion If visual disturbances have not appeared x ray therapy is usually helpful This is especially so if the tumor is a solid chromophobe adenoma Cystic chromophobe tumors do not respond well but fortunately these occur in only a small percentage of cases If visual impairment is present surgical removal is indicated Intractable headache usually responds satisfactorily only to surgical removal of the tumor

Weight should be reduced by a suitable dietary regimen and the hypogonadism corrected by the administration of chorionic gonadotropin as described under Eunuchoidism Females usually do not respond satisfactorily to chorionic gonadotropin and estrogenic substitution therapy is recommended in these cases The dose and method of administration are the same as advised for Primary Ovarian Deficiency Male patients may require testosterone as described under Eunuchoidism

In children gonadotropic and estrogenic substitution therapy should be withheld until the age of 12 or 13 since normal pubertal development may occur

Hypothyroidism is frequently present in these patients and should be corrected by adequate thyroid therapy

Gigantism

Treatment of gigantism follows that described for acromegaly since this condition is also produced by excessive activity of the acidophilic portion of the adenohypophysis occurring before the epiphyses have closed Roentgen irradiation is effective if there is an expanding acidophilic tumor X ray therapy must be given with care to children since there is real danger of damaging the functions of the pituitary Patients with increased visual impairment that is not relieved by x ray therapy should be treated surgically

Eunuchoidal gigantism is occasionally benefited by androgenic or *estrogenic hormone therapy* given in the same manner and dosage as recommended for Acromegaly

In males testosterone propionate in a dose of 50 mg intramuscularly 3 times a week for 4 weeks with subsequent courses at 4 to 6 week intervals until epiphyseal closure occurs and halts the longitudinal growth gives good effect

Pellet implantation of 150 to 300 mg of testosterone subcutaneously into the thigh is effective but must be renewed at approximately 4 to 6 weeks or 6 to 8 weeks depending on the dosage used

CHAPTER LXIX

DISEASES OF THE PITUITARY GLAND

The anatomical position of the pituitary gland and the exceedingly important role it plays in metabolic activities make for a variety of abnormal conditions once the gland has become the seat of disease

Hyperplasia or expanding tumors of the pituitary produce dysfunction by virtue of pressure on adjacent structures or on the remaining normal portion of the gland itself Clinical syndromes may result from either of these conditions or more commonly from a combination of both pressure on the gland and on adjacent structures

The various metabolic functions controlled or influenced by secretions elaborated in the pituitary gland may present, when altered by changes in pituitary activity a variety of abnormal conditions The most clearly recognized clinical entities presented by this altered metabolism are acromegaly, Frohlich's syndrome, gigantism, dwarfism Cushing's disease, Laurence-Biedl syndrome, Sheehan s sydrome, and Simmonds disease

Treatment consists of correcting the altered metabolism and relieving any mechanical pressure on other structures In cases where hyperplasia or an expanding tumor is initiating the difficulty, x ray therapy or sugical removal of the growth is required

Acromegaly

This disease the result of excessive pituitary output after the epiphyses have closed is caused by a tumor or general hyperplasia of the acidophile component of the adenohypophysis Treatment consists of controlling pituitary hyperactivity and relieving anatomical and functional abnormalities brought about by such hyperactivity

Patients exhibiting severe cranial pressure symptoms with marked and rapidly increasing impairment in vision require surgical relief by sella turcica decompression or resection of a portion of the tumor or hyperplastic pituitary gland Prompt surgery in these cases may be life saving and prevent total blindness

although results are not too satisfactory A dose of 50 to 100 rat units of growth factor should be given 3 times a week This dose should be continued 4 to 6 weeks and then a rest period of 4 weeks is to be allowed Patients must be observed carefully and therapy withheld for longer periods of time if growth is excessive or does not slow down properly There should be *6 month observation periods without* therapy, since not infrequently spontaneous growth may appear and continue This plan of therapy should be continued until adolescence if the need is apparent It is of course, of no value in those cases where the epiphyses have closed

When growth is unsatisfactory with administration of anterior pituitary growth hormone it should be supplemented by thyroid extract in the dosage described for *Cretinism If loss of weight nervousness* tachycardia or irritability develops the dose should be reduced Usually a daily dose of 60 mg is adequate

If growth is still unsatisfactory several courses of chorionic gonadotropin 500 international units 2 or 3 times a week for 6 weeks followed by a rest period of 1 month are to be given in addition to the anterior pituitary growth hormone and the thyroid extract Patients must be observed *for abnormal* genital development and therapy discontinued if it appears Male dwarfs approaching puberty may be benefited further by testosterone propionate 25 mg intramuscularly 3 times a week or methyl testosterone 10 to 25 mg sublingually daily for 1 month After a rest period of 1 month the course is repeated Four or five courses a year are recommended

The diet should be high in calories minerals and vitamins, and the *child* should be encouraged to eat heartily *Supplemental vitamins of the* B complex are recommended

Hypogonadal Dwarfism

Treatment should consist of adequate substitution therapy with the appropriate sex hormone Female children showing dwarfism with inadequate gonadal development should *receive ethinyl estradiol* (Estinyl) 0 05 mg by mouth daily Patients must be observed carefully and if abnormal sexual development occurs such as breast or genital enlargement, treatment should be discontinued for 2 weeks and then 0 05 mg given every other day If this therapy does not lead to satisfactory growth and there are no abnormal breast or genital changes the dose may be increased to 0 1 mg daily

day, is helpful in relieving nausea in some of these patients Those who are not relieved of nausea by this drug or by the reduction in the dose of diethylstilbestrol to 0 025 mg daily, should be given ethinyl estradiol (Estinyl), 0 05 mg 1 to 3 times a day, instead of the diethylstilbestrol

Male patients requiring sex hormone therapy should be given testosterone propionate in oil in a dose of 10 to 25 mg intramuscularly 3 times a week until improvement is apparent When the maintenance dose of testosterone propionate has been established, methyl testosterone sublingually may be substituted The daily sublingual dose of methyl testosterone should be approximately 5 times the daily intramuscular dose of testosterone propionate to obtain comparable results Patients must be observed carefully, if jaundice develops, the methyl testosterone should be discontinued and the intramuscular testosterone propionate resumed

Hypothyroidism may occur and require thyroid for relief Treatment with thyroid substance should be cautious, and the patient must be observed closely for signs of adrenal cortical failure Occasionally it is necessary to give extra sodium chloride, desoxycorticosterone, corticotropin and adrenal cortical extract as recommended in the treatment of Addisonian crisis in order to prevent acute adrenal cortical failure in these patients when thyroid medication is pushed

Headache may require analgesics for relief, especially when it is severe Acetylsalicyclic acid, 0 3 to 0 6 gm by mouth 2 or 3 times a day, is helpful Acetylsalicyclic acid combined with acetophenetidin, and caffeine (Empirin Compound), 1 or 2 tablets 3 times a day, is also effective

Skeletal changes, especially prognathism and cervicodorsal kyphosis, may develop and be so severe as to require correction by the orthodontist and orthopedist

If renal calculi develop they must be removed and the patient given large doses of vitamin A, dehydration must be avoided, the urine kept acid, and calcium intake reduced Hyaluronidase (Wydase), 150 TRU in 7 0 cc saline subcutaneously daily, may be helpful in preventing stones See also page 620

These patients must be followed closely and corrective measures applied whenever complications appear Psychotherapy is important and can do much to help the patient adjust

Frölich's Syndrome

This rare syndrome is produced by pituitary dysfunction usually resulting from pressure on the gland by a tumor of the chromophobe cells

Hypofunction of the adrenals is regulated by corticotropin desoxycorticosterone, and sodium chloride as described for Addison's Disease

Hypogonadism responds to appropriate sex hormone therapy and with its improvement the patient is benefited Patients should be started on testosterone propionate 50 mg 3 times a week intramuscularly or methyl testosterone 20 mg sublingually daily, and the dose increased or decreased as the patient s condition indicates Pellet implantation of 150 to 300 mg of testosterone can also be done There should be a gain in weight and increase in strength and appetite In males there is a distinct improvement in the hypogonadism Females will show some masculinization on this therapy

Female patients who do not respond well to methyl testosterone, or who develop virilism are benefited occasionally by vigorous estrogenic therapy If adequate dosage is given secondary sexual characteristics develop and menstruation can be produced The psychological advantage gained by this can be very important A satisfactory course of estrogenic therapy consists of ethinyl estradiol (Estinyl) 0 2 mg or diethylstilbestrol, 1 mg by mouth daily for 1 week the dose doubled the next week tripled the third week and then discontinued for a week Withdrawal bleeding should occur at this time Then, on the third or fourth day of the bleeding the doses recommended for the first week should be given again and the cycle repeated Dosage must be reduced or therapy discontinued if excessive bleeding occurs or the breasts become painful or engorged

Thyroid extract is beneficial in those cases showing pituitary myxedema but care must be taken to avoid production of adrenocortical insufficiency The basal metabolic rate should be checked at monthly intervals until a proper level has been established An initial dose of 15 to 30 mg by mouth daily is to be given and gradually increased as the condition of the patient permits

These patients should receive a diet high in calories proteins, minerals, and vitamins prepared according to individual tastes and desires Every effort should be made to encourage adequate food consumption

The diet should be supplemented by multiple vitamin therapy in the form of Multicebrin 1 capsule by mouth 3 times a day If anemia is present ferrous sulfate or ferrous gluconate 1 to 2 gm by mouth daily is recommended

Psychotherapy is important and should be an integral part of the treatment It can accomplish a great deal in helping these patients adjust to and handle their disease

Females should be given diethylstilbestrol, 5 to 10 mg, for 20 days each month Protective vaccination against such common intercurrent infections as smallpox diphtheria, scarlet fever, and pertussis should be given Adequate rest is essential These individuals are called upon all too frequently to do physical labor far beyond their strength

Headaches, when present, should be treated with acetylsalicylic acid as described for acromegaly

These patients require sympathetic understanding and need help in adjusting to their environment Psychotherapy is a most helpful and important part of any treatment regimen

Dwarfism

Abnormally small stature may be caused by many pathological conditions There are 5 commonly recognized groups of dwarfs (1) primary dwarfs in whom no etiological basis can be established, (2) osteochondral malformation with resultant dwarfism, (3) dwarfism of endocrine origin (4) dwarfism due to metabolic and nutritional disorders and chronic illness, and (5) renal dwarfism

Treatment for all of these must be directed toward relief of the underlying cause and correction of associated deficiencies and abnormalities

Primary and osteochondral dwarfism resist treatment Such individuals should be informed of the possible role of heredity in reproducing their condition

Dwarfism of endocrine origin may result from hypothyroidism (cretinism) hypopituitarism and hypogonadism either as the primary factor or in conjunction with one another, or from other conditions contributing to underdevelopment in stature

Hypothyroid Dwarfism

The treatment for this condition is the same as that advised for Cretinism

Hypopituitary Dwarfism

Treatment is not satisfactory, but definite improvement can be secured in some cases if the diagnosis is made early and therapy is started promptly

Anterior pituitary lobe extract given parenterally should be tried

CHAPTER LXX

DISEASES OF THE GONADS

Alteration in function of the gonads produces several well recognized syndromes and a variety of ill defined poorly recognized but probably associated conditions Hypogonadism in the male depending upon the degree of deficiency, produces eunuchism eunuchoid states and the male climacteric In the female hypogonadism causes the climacteric or menopause and may contribute to such conditions as amenorrhea, hypomenorrhea oligomenorrhea and dysmenorrhea Hypergonadism is rare and when seen is usually the result of a tumor or abnormal function of glands other than the gonads

Tumors either benign or malignant may occur in both sexes In the female the granulosa cell tumor and the thecal cell tumor are capable of producing feminizing effects The former may be bilateral, and some of them are malignant Occasionally the granulosa cell tumor occurs in childhood and causes precocious puberty Arrhenoblastomas adrenal rests luteomas and rarely a dysgerminoma can cause masculinizing effects Other rare tumors with hormonal capabilities are the struma ovarii which occurs as a part of a teratoma and is composed of thyroid tissue capable of producing hyperthyroidism and chorio-epitheliomas, which can produce premature puberty in childhood accompanied by severe uterine bleeding

In the male the testes may not descend into the scrotum during the normal course of development and cryptorchidism results Orchitis, either acute or chronic and atrophy may follow infection trauma or exposure to x ray

Eunuchism

Castration or complete destruction of the testes produces complete hypogonadism with the characteristic pattern of eunuchism Treatment of this condition consists of adequate substitution therapy with testosterone In the rare case of eunuchism occurring before puberty the treat-

Girls showing hypogenitalism at the time of puberty may be given larger doses without producing physiological and psychological trauma These patients should receive relatively larger doses for a brief period in order to induce the maximum degree of development at this time Usually a dose of 0 2 to 0 3 mg daily is sufficient to produce menstruation or adequate genital development The hormone is to be discontinued when either appears

In male hypogonadal dwarfs, testosterone propionate, 25 mg 3 times a week, or methyl testosterone, 10 to 25 mg daily sublingually, is recommended The patient must be observed closely and development followed carefully After 2 or 3 months of treatment the hormone should be withheld and the growth curve watched When development falls off the hormone should be resumed in the same dosage Hormone therapy with periods of observation without medication should be continued in this manner until the epiphyses are closed or until normal growth and development have occurred

Metabolic and Renal Dwarfism

Treatment should consist of correction of the underlying cause when possible along with measures directed toward stimulating growth and development Infections should be eliminated by proper antibiotic therapy Nutritional deficiencies should be corrected by an adequate diet high in vitamins minerals and calories

Bronchiectasis, congenital cardiac lesions, any obstruction of the urinary tract and other surgically correctable abnormalities interfering with normal growth should be remedied When acidosis is present, some relief may be secured from Shohl's solution This consists of 140 gm citric acid and 98 gm sodium citrate in 1000 cc of water Patients should take 50 to 100 cc of the solution daily

Sheehan s Syndrome and Simmonds Disease

Endeavor to find the cause of the pituitary malfunction and remove it if possible Tumors syphilitic gummas cysts abscesses tuberculoma and many other conditions may involve the gland directly or impair its function by pressure on it or its blood supply

Substitution therapy with pituitary extract is unsatisfactory Such treatment is expensive, and the extract lacks sufficient potency to control the disease

action of chorionic gonadotropin should be ascertained before androgen therapy is started

Treatment of eunuchoidism in young boys should be begun sufficiently early to secure normal growth and development Usually the time of puberty ages 10 to 12 years is the most favorable time to start therapy in juveniles

If the hypogonadism is caused by a lack of pituitary gonadotropin the pituitary gland should be investigated carefully for a tumor or other defect and remedial measures applied Treatment with chorionic gonadotropin 750 international units intramuscularly twice a day for 4 to 6 weeks, is helpful followed by one half this dose for the next . months A rest period of 3 to 6 months is then given If regression occurs another 3 month period of treatment and a subsequent 3-month rest period should be given This cycle may be repeated as needed Testicular stimulation with chorionic gonadotropin should produce normal growth and development Secondary sex characteristics should appear gradually together with improvement in appetite weight and strength If definite improvement is not seen with this treatment testosterone propionate or methyl testosterone should be given If there is evidence of some testicular function the dose of testosterone should be adjusted to supply the deficiency Testosterone propionate 25 mg intramuscularly 3 times a week or methyl testosterone 10 to 20 mg sublingually 3 times a week is a satisfactory starting dose The dose should then be adjusted to the patient s needs

Patients with testicular defect as the cause of hypogonadism and those who do not respond to chorionic gonadotropin should be given testosterone propionate 5 to 50 mg intramuscularly 3 times a week, or methyl testosterone 15 to 50 mg sublingually 3 times a week

Occasionally hypothyroidism is also a factor in eunuchoidism If present it should be corrected by adequate thyroid therapy

Male Climacteric

Withdrawal or decreased elaboration of male sex hormone occasionally produces this symptom complex It is a diagnosis arrived at only after careful study and exclusion of many other conditions with which it can be confused Treatment consists of thorough diagnostic studies followed by a careful explanation of the condition to the patient and the administration of adequate testosterone therapy

Most patients are relieved by testosterone propionate 25 mg intra-

Infections must be treated promptly with the proper antibiotic therapy Whenever possible the individual should be immunized protectively against infectious disease Minor illnesses, trauma, and mental and physical strain are dangerous and may precipitate adrenal cortical failure If this should occur, treatment as advised for Addison's Disease is recommended

Hypophyseal Basophilism Cushing's Disease

Treatment for this disease is the same as that recommended for Cushing s Syndrome

Laurence-Moon-Biedl Syndrome

There is no effective treatment for this syndrome Dietary restriction to prevent obesity, or loss of weight if obesity has already appeared is recommended Young patients may be benefited by 500 to 1500 units of chorionic gonadotropin intramuscularly 3 times a week for 6 weeks After a rest period of 2 months the course may be repeated Usually there is no response to this therapy, and when such is the case estrogens and testosterone as recommended for Frohlich's syndrome should be given Thyroid extract is helpful to some patients A daily dose of 15 mg increased to 60 mg is usually satisfactory

BIBLIOGRAPHY

Diseases of the Pituitary Gland

1 BUTT A J and HANSEN, E A 'The Importance of Protective Urinary Colloids in the Prevention and Treatment of Kidney Stones *Science* 1952 cxv, p 308
2 HAMBLEIN, E C *Endocrinology of Women*, Charles C Thomas, Springfield 1947
3 HURXTHAL L M 'Treatment of Gigantism Observations on a Pituitary Giant for Six Years ' *J Clin Endocrinology*, 1943 iii p 12
4 SOFFER L J *Diseases of the Endocrine Glands*, Lea and Febiger, Philadelphia, 1950
5 SOSMAN, M C 'The Roentgen Therapy of Pituitary Adenomas," *Jour Amer Med Assoc* 1939 cxiii p 1282

When surgery is decided upon the operative procedure of *Gross* is recommended Certainly procedures fastening the testes to the thigh or putting strain on the circulation are undesirable and may actually lead to sterility

If, after surgery inadequate development of the genitals or other evidence of hypogonadism occurs it should be treated as recommended on page 819 This complication fortunately is very rare therefore it is necessary to insure the correct diagnosis by measuring levels of urinary gonadotropin and androgen excretion before treatment is started If hormone therapy is given care must be taken to prevent a precocious puberty Since there is frequently considerable emotional tension associated with cryptorchidism both in the minds of the parents and the boy involved psychotherapy is important and should never be neglected

Ovarian Dysfunction

Ovarian activity may be disturbed by many conditions such as endocrine disbalance elsewhere in the body infections metabolic disorders and psychogenic factors Also it may be disrupted primarily as a result of ovarian malfunction Hypoactivity either primary or secondary produces hypogonadism and atrophic vaginitis and vulvitis depending on the age of the patient and the degree of hypofunction Hyperactivity may produce functional uterine bleeding Some neoplasms of the ovary produce endocrine changes The arrhenoblastomas adrenal rest tumors luteomas and rarely the dysgerminomas produce masculinizing effects Granulosa cell and thecal cell tumors can cause feminizing effects

Treatment for ovarian dysfunction is divided into general measures applicable to most cases and those directed toward relief of the specific disorder Therapy must be preceded by a thorough diagnostic study and accurate evaluation of the patient s condition

General Measures Infections dietary abnormalities and metabolic disturbances must be attended to promptly and unhygienic activities must be stopped Psychogenic disturbances may present a serious obstacle to successful treatment and vigorous well thought out intelligent psychotherapy is frequently most helpful If hypothyroidism is present correction of this condition with adequate dosage of thyroid extract will give excellent results Thyroid extract is of little or no value in the absence of hypothyroidism and its empirical use in these

ment should be the same as that described for eunuchoidism except that preliminary trial with chorionic gonadotropin is unnecessary.

In the adult testosterone propionate, 25 mg intramuscularly 3 times a week, is recommended and usually gives satisfactory results. Occasionally it is necessary to give as much as 50 mg 3 times a week to secure maximum benefit.

Methyl testosterone by mouth is effective in a dose of 30 to 100 mg in divided doses before meals 3 times a week. It can be given also sublingually, with excellent results, in a dose of 15 to 50 mg. When it is given sublingually, the patient must be instructed to allow at least 1 hour for the dose to be absorbed and to swallow all saliva during this period.

Pellet implantation has been used with success, but as yet there has been insufficient experience with this route to be sure of maximum benefit. In those cases where it seems desirable, pellets of testosterone may be implanted after the maximum development has been attained by the intramuscular or oral route. A dose of 0.2 to 0.5 gm deposited by a trocar into the subcutaneous tissue on the inner aspect of the thigh is recommended. Implantation of similar amounts must be repeated at 5- to 8 month intervals.

These patients usually have serious psychological as well as physical handicaps and are in need of skilled psychotherapy. Every effort should be made to help them adjust to their environment. Usually with adequate testosterone therapy they are able to undertake normal activities in all aspects of everyday life.

Eunuchoidism

When the testes are still capable of secreting some testosterone but in greatly reduced amounts, the condition of eunuchoidism exists. The hyposecretion may result primarily from a defect in the testes or secondarily from a lack of pituitary gonadotropic hormone with resulting failure of testicular stimulation. Hormonal assay of the urine will show a low or absent gonadotropic hormone content in secondary eunuchoidism but will be normal in primary testicular defects. If the hormonal assay cannot be made, the administration of 750 international units of chorionic gonadotropin intramuscularly 2 times a day for 3 weeks will produce testicular stimulation if the defective secretion is due to a lack of pituitary gonadotropin. If the defect is in the testicles the response to the chorionic gonadotropin will be unsatisfactory or negative. The

(Estinyl), 0 05 mg 3 times a day by mouth, is excellent Water soluble estrogenic substance (Premarin) 1 25 to 3 75 mg by mouth daily, is effective also Diethylstilbestrol in a daily dose of 0 2 to 1 0 mg orally is also satisfactory but is more prone to produce toxic side reactions Treatment is very effective, and within 3 to 6 months sexual characteristics become normal epiphyses close and the eunuchoidal features lessen or disappear

Patients with hypogonadism who have what appear to be normal ovaries should have artificially induced rhythmic bleeding in the hope that cylical bleeding will appear and continue in the normal fashion after the hormones are withdrawn Artificial cyclical bleeding may be induced by the administration of ethinyl estradiol (Estinyl) 0 05 mg by mouth 3 times a day, or water soluble estrogenic substance (Premarin), 1 25 mg by mouth 3 times a day or diethylstilbestrol, 0 5 to 1 0 mg a day for 20 days during the last 10 of which the patient also receives progesterone 25 mg every other day At the end of withdrawal bleeding the course is repeated After 3 courses have been given treatment is discontinued for 3 to 6 months Occasionally normal cyclical bleeding is started by this therapy If regression occurs estrogenic cyclic therapy is repeated Unfortunately the majority of patients fail to show any permanent benefit

Ovarian Dwarfism

Treatment for this syndrome is estrogenic substitution therapy as recommended for hypogonadism Complete sexual maturation will usually be secured in a period of from 3 to 6 months The epiphyses should close and eunuchoidal characteristics disappear It is not advisable to induce cyclical bleeding artificially in these patients for normal bleeding and pregnancy are impossible because of the primary ovarian deficiency

Bilateral Polycystic Ovaries (Stein Leventhal)

This syndrome characterized by amenorrhea, sterility, hirsutism of varying degrees pain rarely and menometrorrhagia occasionally may be helped appreciably by wedge shaped resection of the ovaries Menstruation may return in 75 per cent of cases and conception may follow in 65 to 75 per cent In only a few may the hirsutism be decreased by this surgical procedure

muscularly 3 times a week Methyl testosterone may be tried in a dose of 20 to 40 mg daily sublingually, but it is not as effective If jaundice appears, it must be stopped When the patient has been controlled adequately, pellet implantation can be instituted if desirable Satisfactory results are usually secured when 4 to 8 pellets containing 75 mg each are implanted into the inner aspect of the thigh, 3 or 4 pellets into each thigh Reimplantation is usually necessary every 6 to 10 months

Cryptorchism

Failure of the testes to descend into the scrotum can, if not corrected, lead to sterility, consequently steps should be taken to relieve the condition before puberty Cryptorchism may result from anatomical defects blocking the normal descent of the testicles, from endocrine disbalance with underdevelopment of the genitals, and may occur also in patients with apparently no anatomical or endocrine defects to account for the condition Certainly delay in descent of a testicle is not uncommon Usually with the onset of puberty testes capable of descending, do so Occasionally a testicle which has never been in the scrotum will descend after almost all hope for it descending unaided has been abandoned Unfortunately confusion arises when puberty is delayed until 16 or 17 years as is the case in a limited number of boys

Since sterility will result if the testes have not descended before puberty, it is necessary to give treatment early enough to insure their being in the scrotum by that time In the vast majority of cases treatment should start between the ages of 8 and 10 years so that there will be sufficient time for surgery if endocrine therapy should fail Although sterility will not result if only one testicle is undescended, the possibility of malignancy or trauma occuring is certainly greater and this, plus the psychological problem presented, make it desirable to correct unilateral crytorchidism

Chorionic gonadotropin (Antuitrin S) 500 to 1000 international units intramuscularly 3 times a week for 6 weeks is adequate If the testis has not descended by this time and fails to do so in the next month, a surgical approach is indicated Some prefer giving chorionic gonadotropin in a dose of 4000 to 5000 international units daily for 3 days and if there is no change in the position of the testis within a week surgery is recommended

by adequate substitution therapy with female sex hormone A thorough check of the breasts genitals uterus and ovaries to rule out any possible neoplastic condition must be made before commencing any sex hormone therapy *Breast masses and fibromyomata of the uterus are contraindications to the use of estrogen* There are many preparations available for both intramuscular and oral routes of administration. There is rarely any real advantage to be gained by intramuscular injections, which are both costly and inconvenient to patient and physician Administration by the *oral route is the method of choice in the great majority of these* patients The highly potent orally effective ethinyl estradiol (Estinyl) is recommended The dosage must be adjusted to the patient s needs It is preferable to start with smaller doses 0 02 to 0 05 mg twice a week at bedtime and gradually increase the dose until the minimal amount *that will control the symptoms is reached* Usually 0 05 mg *every other* evening is sufficient Occasionally 0 05 mg each evening is required to secure adequate relief Water soluble estrogenic substance (Premarin) 0 65 to 1 25 mg, by mouth, is also effective The cheaper synthetic di ethylstilbestrol in a dose of 0 2 to 0 5 mg a day by mouth is effective but occasionally produces toxic side effects and does not give the sense of well being often felt during therapy with Estinyl and Premarin Di ethylstilbestrol also tends to produce nausea somewhat more frequently than the other preparations in the higher dose ranges

Patients *receiving estrogenic substitution therapy must be observed* closely Overdosage must be avoided and the dose level should be kept as low as possible while still producing the desired effects The estrogen should be continued in minimal dosage for several months and then an attempt should be made to reduce or discontinue the hormone *Usually treatment must be continued for 6 months to a year or even longer* It is better for the patient to be on regular minimal dosage than to take larger amounts at irregular intervals The hormone should be discontinued as soon as the patient s condition permits

Any vaginal bleeding or the appearance of any suspicious change in the breasts genitals uterus or ovaries must be checked carefully and, until the nature of the lesion is known the drug should be discontinued The possibility of carcinomatous degeneration being the cause of such bleeding must be kept in mind constantly *If bleeding persists after withdrawal of the estrogen* dilatation and curettage is indicated

Atrophic Vaginitis and Vulvitis

Inadequate estrogenic activity may lead to atrophic vaginitis with

cases is usually disappointing

Therapy with sex hormones is adjusted to suit the specific need. In general it consists of ovarian stimulation by gonadotropic hormone, substitution therapy with ovarian hormone, and the use of androgens to suppress female sex function

Ovarian Hypofunction

Treatment of ovarian hypoactivity is determined by the type of dysfunction present and by whether the hypoactivity is primary in the ovary or secondary to pituitary hypogonadotropic activity Unfortunately ovary-stimulating hormones are not usually very effective even when the hypoactivity is secondary to a lack of normal pituitary gonadotropin

Hypogonadism of Female with Amenorrhea

The patient should be studied thoroughly and the degree of development of secondary sex characteristics and the titer of gonadotropic excretion determined If these studies show that gonadotropic hormone is deficient, thus indicating a secondary hypogonadism, stimulation of the ovary with a hormone should be tried For this purpose equine gonadotropic hormone is recommended The patient must be checked carefully by a skin or conjunctival test to rule out any allergy to the preparation Failure to do this before the initial and subsequent injections may result in a serious anaphylactic reaction If there is no allergy to the hormone, a dose of 200 to 400 international units 3 times a week for 2 weeks followed by a rest period of 2 weeks is advised The course of treatment is repeated and continued in this manner for 3 months and then a rest period of 3 months is allowed The course is then repeated with double the previous dose of the hormone If allergy prohibits the use of equine gonadotropin, chorionic gonadotropin in a dose of 500 international units intramuscularly 3 times a week in the same manner as recommended for the equine hormone may be given If improvement is not apparent with this treatment, substitution therapy with estrogenic substance as recommended for primary ovarian hypofunction is advised

When the gonadotropic hormone excretion is found to be normal, as is usually the case, primary ovarian deficiency exists, and substitution therapy with the estrogenic hormone is necessary Ethinyl estradiol

age of 45 years not desirous of having more children completely abolishing ovarian function by x ray radiation gives excellent results In younger patients, organotherapy must usually be carried out

Estrogen therapy frequently gives good results diethylstilbestrol, 3 mg daily by mouth ethinyl estradiol (Estinyl), 0 1 mg by mouth 3 times a day or water soluble estrogenic substance (Premarin), 2 5 mg by mouth 3 times a day is recommended If bleeding has not decreased in 3 or 4 days the dose should be increased by 50 percent If curettage has been performed estrogenic therapy as just described is to be commenced on the third day but only in about half that dosage The estrogens are to be continued in the dosage found satisfactory to produce hemostasis for 3 weeks The hormone is then withheld for 1 week during which time withdrawal bleeding occurs Estrogen therapy is then to be resumed for another cycle and this routine is to be repeated for 3 or 4 cycles Occasionally better results are secured with anhydrohydroxyprogesterone (Progesterol), 10 to 30 mg daily by mouth or progesterone, 10 mg intramuscularly every other day given for the 10 days preceding the withdrawal of estrogen during each cycle If regular normal cycles are not re established or satisfactory hemostasis secured by this therapy or by increased dosage of estrogens through 6 or 8 cycles testosterone should be given If bleeding is severe and not controlled by estrogen therapy testosterone should be given for the immediate control and then attempts should be made to re establish the normal menstrual pattern

In severe menorrhagia with profuse bleeding testosterone propionate 25 mg daily intramuscularly for 3 to 5 days or methyl testosterone orally or sublingually 20 to 40 mg daily for 3 to 5 days, will usually control the bleeding The hormone should then be continued for a few cycles but if possible a total dose of 250 mg of testosterone or 700 mg of methyl testosterone a month should not be exceeded as doses of this order or less seldom cause masculinizing effects The hormone should be discontinued as promptly as possible and the dose reduced to the smallest amount that can control the hemorrhage The use of small daily doses 10 mg of methyl testosterone sublingually, will frequently control irregular functional bleeding or reduce profuse or prolonged bleeding at the menses Testosterone tends to depress the entire cycle and of course produces male sex changes if given in sufficiently large doses over a period of several months Patients must be observed carefully and the hormone discontinued or reduced in dosage if untoward effects

Female Climacteric Menopause

Management of the female climacteric is based upon the proper diagnostic evaluation, adequate female sex-hormone therapy, and measures designed to relieve fear and psychic tension Patients presenting the signs and symptoms of menopause should be studied carefully and a correct diagnosis made before therapy is commenced

The most important factor in treatment consists of relieving the patient of the usual and often severe emotional factors A careful explanation of the nature of the climacteric, the fact that it does not mean the end of sexual activity or the onset of feebleness and old age, and that there will be no undesirable physical developments, is most helpful Patients should be reassured about hot "flashes" and other vasomotor hyperactivity and be encouraged to continue with normal mental and physical activity The fear of cancer or mental disease is often present and should be removed

Patients with mild vasomoter disturbances, irritability, nervousness, insomnia, or emotional tension are frequently relieved by small sedative doses of phenobarbital, 15 mg by mouth 4 times a day Care must be taken to avoid oversedation or chronic addiction. Hot flashes are annoying and create considerable emotional tension and fear A careful study of the patient's habits, environment, and personality is helpful and often gives information of value in controlling this symptom The patient may be wearing too heavy clothing, exercising too vigorously, or subjecting herself to useless emotional strain and irritation—all of which may bring on or increase the frequency of these attacks Mild sedation is helpful in controlling hot flashes when they are caused by emotional tension Gastro-intestinal disturbances may appear and require mild antispasmodic, antacid treatment Tincture of belladonna, 0 6 cc by mouth 3 times a day is helpful if spastic symptoms are present Aluminum hydroxide and magnesium trisilicate (Gelusil) tablets, permitted to dissolve slowly in the mouth, may be soothing and relieve gastric distress If headache is a prominent feature, acetylsalicylic acid, 0 3 to 0 6 mg is recommended Often well-organized psychotherapy and the occasional use of sedatives are all that are required to secure relief from the manifestations of this syndrome

The patient with severe vasomotor and emotional disturbances that do not respond to the foregoing measures—who may have these symptoms to such a degree as to be incapacitated by them—is often relieved

I

PART XX

DISEASES OF THE MUSCULO SKELETAL SYSTEM

The diseases of the muscles, tendons, and adipose tissue comprise a rather wide variety of clinical entities of diverse etiology, often unknown, with involvement of muscles, tendons, cartilages and bones These will be discussed under diseases of the muscles and tendons diseases of the joints, and diseases of the bones and cartilages

CHAPTER LXXI

DISEASES OF THE MUSCLES AND TENDONS

Myositis

Myositis is an inflammation of striated skeletal muscle, and may be acute, subacute or chronic, suppurative or non suppurative, primary or secondary, localized or extensive

The treatment of simple, acute, non suppurative myositis such as occurs after exposure to cold, in the course of a respiratory infection, or after trauma should consist of immobilization of the muscle or muscles involved, with the application of warm, preferably wet heat, and the use of salicylates and sedatives for pain The salicylates, either sodium salicylate or acetylsalicylic acid, are to be given as outlined for Acute Rheumatic Fever Occasionally local spasm is relieved by 2 or 3 sprayings with an ethyl chloride spray Infiltration of a local spastic area with 2 per cent procaine hydrochloride may break up a local spasm and give relief

Prednisone (Meticorten) 5 to 10 mg every 6 hours is helpful especially when given concurrently with salicylate therapy Muscle spasm is usually not relieved by drug therapy Mephenesin (Tolserol) 3 to 5 gm daily by mouth and meprobamate (Equanil) 0 4 to 0 8 gm every 6 hours may be tried but usually do not prove very helpful Zoxazolamine (Flexin) 0 5 gm 3 or 4 times a day has also recently been shown to give

its attendant irritation, leukorrhea, pruritus, and dyspareunia Often associated with the vaginitis is a chronic vulvitis, resulting in part from scratching to relieve pruritus, and also trophic changes in the skin

Treatment consists in giving adequate estrogenic therapy Ethinyl estradiol (Estinyl), water soluble estrogenic substance (Premarin), or diethylstilbestrol are all effective in relieving the symptoms of atrophic vaginitis They should be given as vaginal suppositories or as water soluble creams applied to the vulva and inserted into the vagina Oral therapy with ethinyl estradiol (Estinyl) 0 02 mg daily by mouth, estrogenic substance (Premarin), 0 625 mg orally each day, or diethyl stilbestrol, 0 5 mg by mouth daily, is also effective and preferred by some patients Treatment should be continued for approximately 1 month The treatment is to be repeated if a relapse occurs The carbohydrate content of the diet should be reduced, and if diabetes mellitus is present, it must be controlled carefully

Antihistaminics by mouth frequently relieve the pruritus temporarily Tripelennamine (Pyribenzamine) hydrochloride or diphenhydramine (Benadryl) hydrochloride, 25 to 50 mg, by mouth 3 or 4 times a day, is often helpful Topical applications should usually be avoided

Vaginal douches with physiological salt solution or douche solution made acid with white vinegar once or twice a week removes discharge and reduces irritation Frequent douches are not advised, since removal of normal secretions too often promotes irritation

Functional Uterine Bleeding

Excessive bleeding at the menses, prolonged menstrual periods, or almost continual bleeding requires thorough study and skilful management

Infections emotional tension, overfatigue, malnutrition, dietary deficiencies, anemia, hypothyroidism, and other possible causative or complicating conditions must be relieved

Curettage is recommended for diagnostic and therapeutic purposes, especially if bleeding is severe or is occurring in females after the age of 35 years In girls and younger women with profuse bleeding that requires hemostasis, it may be necessary to resort to surgical packing of the uterus and vagina

When diagnostic studies indicate that the bleeding is resulting from endocrine imbalance, at attempt to bring about a readjustment of hormone activity should be undertaken In menopausal women, over the

hormones biopsy studies of involved muscles have shown little or no change or at most a temporary remission

Some benefit in dermatomyositis has been seen to occur after the use of testosterone propionate, either by intramuscular injection or by pellet implantation More recently however the evidence suggests that this treatment may be more effective when instituted after a course of cortisone or corticotropin The testosterone may be administered in an oil preparation intramuscularly 50 mg twice a week, or by the implantation of 3 or 4 testosterone pellets, each of 100 mg size or by the oral administration of 10 mg tablets sublingually 5 times a day In children the dosage of testosterone should be correspondingly smaller one half to two-thirds of the adult dose outlined above In females a total dosage of 200 to 300 mg per month may be given for a rather indefinite period without fear of masculinization

Para aminobenzoic acid has been tried on the basis that some patients with dermatomyositis are photosensitive The results of such treatment have been variable but for the most part disappointing para aminobenzoic acid in doses of 2 to 3 gm by mouth every 2 to 3 hours for a total daily dose of 18 to 24 gms may be given a trial Patients who demonstrate photosensitivity should avoid the sunlight For any existing anemia, transfusions of whole blood should be given since liver and iron therapy are not often effective Physiotherapy especially moist heat passive motion and exercises, as indicated are beneficial The use of neostigmine (Prostigmine) methyl sulfate, 1 2000 intramuscularly daily in a dose of 1 0 cc, often gives some relief During acute exacerbation penicillin seems to help Therefore it as well as other antibiotics should be given a trial *Careful watch should be made for the development of* complications such as pneumonia phlebitis pyelitis and these if they occur, should be treated promptly by an antibiotic found effective against the causative organism During the acute phase of dermatomyositis some advocate the use of penicillin in full dosage as a preventive *measure against complications*

Myositis Ossificans

The treatment of myositis ossificans is entirely symptomatic salicylates should be given in full dosage as analgesics if there is pain and discomfort A localized form of myositis ossificans following trauma the Pelligrini Stieda syndrome may be benefited by deep roentgen

appear As a last resort surgical removal of the uterus may be necessary

Tumors of the ovary are usually malignant or are capable of undergoing malignant degeneration, and therefore, once this diagnosis is made, surgical removal is indicated

BIBLIOGRAPHY

Diseases of the Gonads

1 HAMBLEN E C *Endocrinology of Women*, Charles C Thomas Springfield, 1947
2 HELLER, C G, and NELSON, W O 'Male Hypogonadism," *J Clin Endocrinology*, 1948, VIII, p 345
3 NOVAK, E 'Functional Gynecological Diseases," *Oxford Medicine*, Vol III Part III, Chapter XVIII, p 1027
4 SOFFER, L J *Diseases of the Endocrine Glands*, Lea and Febiger Philadelphia, 1950
5 GROSS R E., and JEWETT, T C 'Surgical Experiences from 1,222 Operations for Undescended Testis," *J A M A*, 1956, CLX, 634
6 GREENBLATT, R B The Syndrome of Large, Pale Ovaries and its Differentiation from Adrenogenital Syndrone and Cushing s Disease, *Post Grad Med*, 1951, IX, 492

bursa With calcified subdeltoid bursitis local excision should not be attempted for recurrence is the rule

Five or six or more high voltage roentgen ray treatments on the other hand, are useful in the majority of patients In most cases physical therapy with heat, massage, and stretching exercise is very useful For the low back pain a wide lumbo sacral corset, properly fitted, is most useful The belt should be worn the entire day but removed at night The patient should sleep on a firm felt mattress with table leaves or a veneer bed board placed between the mattress and springs to provide firm support to the back muscles Some mattresses are now being manufactured for just such purposes Inner-spring mattresses should be avoided

Corrective exercises are helpful Muscles of the abdomen and back should be strengthened by leg raising exercises while the patient is lying on his back on the floor A tight fascia lata band may be tipping the pelvis forward thus causing pain in the lower back This may be corrected by exercise designed to stretch the band have the patient stand sideways and lean against a wall while bending at the hips with the knees held straight in a lateral direction so as to bring a distinct pull on the fascial band Both sides are stretched during each exercise period Usually 15 or 20 bends are sufficient each time and the exercises should be done twice a day

For another form of chronic fibrositis Dupuytren s contractures alpha tocopherol [vitamin E] has recently been advocated, but in our experience with doses of 300 to 400 mg a day it has been of no benefit For the patient with mild to moderate contracture no treatment need be given but corticotropin, 25 mg daily or cortisone 50 to 100 mg daily may be tried In the more severe form with a handicap deformity surgical correction followed by adequate skin grafting is the therapy recommended

Myotonia Atrophica Dystrophia Myotonica

Although at present there is no effective cure of this condition frequently much can be done in the way of supportive treatment The recent introduction of quinine for this disease has proved most helpful since the myotonia can be diminished materially by the use of 0 6 to 2 0 gm of quinine sulfate by mouth daily The course of the disease is not influenced by quinine however Gonadal atrophy may be alleviated

some relief from muscle spasm It may be quite toxic, however, frequently causing nausea and vomiting

In many of these cases there is an important psychological factor, fear of arthritis, emotional tensions from many causes and muscle tension from emotional factors all contribute to the problem Therefore, it is important to correct these factors if satisfactory results are to be secured.

In chronic myositis, search should be made for any anatomical structural deformity and if such is found, proper corrective measures should be instituted to relieve muscle irritation When the process is a suppurative one, either primary or from adjacent infection, the presence of fluctuation calls for incision and drainage followed by the institution of full courses of antibiotics directed against the infecting organism, along with local heat and analgesics A phlegmonous process, such as in erysipelas, should not be incised For the myositis of trichinosis there is no specific treatment Early in the trichinella infection a brisk purge should be given to rid the intestines of any remaining parasites If the patient is very ill or has severe muscular pains, complete bed rest should be instituted with the use of salicylates for pain as outlined above Careful observation for complications should be made, particularly for cardiac involvement, and if found, they should be treated by appropriate measures The treatment of myositis of syphilis is the same as that for systemic syphilis

Dermatomyositis

Although some new measures have been introduced for the therapy of dermatomyositis there is as yet no specific cure Treatment should begin with symptomatic measures bed rest if indicated, a high protein, high-vitamin diet, supplemented orally by amino acids (Powdered Amigen, Powdered Lactamin), 60 to 100 gm a day, and multivitamin therapy with vitamin B complex (Lederplex) and ascorbic acid, 500 mg per day Patients with respiratory muscle involvement may be benefited considerably by oxygen therapy Salicylates are also occasionally of benefit In a few cases, particularly in younger individuals, before extensive vascular and connective tissue changes have taken place, corticotropin or cortisone has been found to be effective Corticotropin should be given in doses of 10 to 25 mg every 6 hours for several weeks, cortisone in doses of 50 mg every 6 hours for the same period of time Although much benefit has been reported from steroid

attack, when relatively large doses of neostigmine may be required such side effects as gastro-intestinal and uterine cramps may occur If the condition of the patient does not allow for a reduction in dosage, such side effects should be combatted with the use of atropine sulfate, 0 4 to 0 6 mg subcutaneously or orally every 4 hours Some advocate the combined used of ephedrine sulfate 24 mg with each dose of neostigmine bromide to help in overcoming weakness in mild cases but ephedrine guanidine, potassium salts and glycine have lost favor in the treatment of the acute episodes of myasthenia gravis

A concomitant infection should be treated with antibiotics and chemotherapy in full dosage chosen for specificity against the invading organism Respiratory failure should be treated with the administration of oxygen and the use of a respirator if needed

In crises of myasthenia gravis neostigmine methylsulfate should be given intravenously every hour in doses of 0 5 to 1 5 mg as long as necessary

In the *continuous treatment* of myasthenia gravis neostigmine (Prostigmine) bromide, 15 mg tablets regulated in dosage and time intervals to meet the individual requirements, can be continued indefinitely It has been found to be effective in 85 per cent of the cases Variations in dosage need to be made from time to time however, and some patients develop a tolerance to the drug that requires such increase in dosage as to make the cost almost prohibitive The average case requires in the end about *165 mg of the drug daily Some cases need much more* For these reasons and because thymectomy or radiation therapy of the thymus gland has been found to be effective they should be given serious consideration in each case All agree however that thymectomy is not uniformly successful in this disease It appears to be less useful when there is a thymoma At the present time thymectomy is thought to be most effective in the early case—i e of less than one year s duration—particularly young females who are not on very large doses of neostigmine for any long period of time The post operative course may be stormy, requiring oxygen administration the use of respirator parenteral neostigmine careful nursing care and sometimes tracheotomy These factors coupled with an unpredictability of remissions, causes us to advise against thymectomy as a routine procedure in the treatment of myasthenia gravis The very mild case may with great caution be given quinine or curare or the quartenary ammonium compounds as a test dose as an aid in establishing the diagnosis but great care should be

therapy locally Local excision of the Pelligrini Stieda calcification should not be attempted since recurrence is usual

Fibrositis

Fibrositis, or fibromyositis is an inflammation of fibrous tissue that may be acute, subacute, or chronic, occurring anywhere in the body It may be localized in muscles, sheaths, ligaments, tendons, fasciae, and bursae, giving rise to such terms as myalgia, synovitis, tenosynovitis, bursitis, and perineuritis The condition may be primary or it may be secondary to such conditions as rheumatic fever, gout rheumatoid or hypertrophic arthritis, and gonorrhea Whether primary or secondary the treatment of the manifestations of fibrositis is the same

Once the diagnosis is established, foci of infection should be sought for carefully—in the teeth, tonsils, and paranasal sinuses especially for a fibrositic condition about the head, neck, shoulders, and arms, and in the prostate, cervix, and other pelvic structures for fibrositis involving the hip regions and lower extremities

When possible the affected part should be immobilized, certainly unnecessary motion of the part should be avoided This pertains particularly to subachromial bursitis which may be helped greatly in the acute stage by the proper application of a sling to the arm Sudden changes of temperature, particularly cold, should be avoided Local heat, applied intermittently, is very useful The pain, which may be very disabling should be treated by adequate doses of salicylates, either as sodium salicylate or acetylsalicyclic acid, 0 6 to 1 0 gm every 3 to 4 hours Some patients are helped further by the local application of either methyl salicylate [oil of wintergreen] or chloroform liniment once or twice a day Mild dry heat may be applied after these with further benefit Sometimes in the acute phase of bursitis, especially in the more common subachromial type, high-voltage roentgen therapy will be quite effective in relieving the pain Spraying the area with ethyl chloride may help relieve a local spasm If the pain persists after such measures resort may be had to the use of meperidine (Demerol) hydrochloride, 50 mg, or even morphine sulfate, 8 to 15 mg as necessary When the site of pain is well localized, injection of 5 to 10 cc of a 2 per cent solution of procaine (Novocain) hydrochloride into the site is very useful, or the injection of 5 to 15 mg of hydrocortisone acetate into the inflamed bursa, this is done through needle puncture of the

this new drug shows promise It should be tried particularly in cases that do not respond satisfactorily to neostigmine An oral dose of 5 to 25 mg 3 times a day is recommended Occasional patients will require 50 to 75 mg at a dose In the present state of knowledge the dosage for parenteral administration of ambenonium is too variable and the parenteral use is not advised

Recently four phosphate compounds with strong cholinesterase inhibiting properties have been introduced for the treatment of myasthenia gravis Three of these are of no value in therapy The fourth, tetraethylpyrophosphate (tepp) has a longer action than neostigmine—24 to 36 hours when given as a 1 per cent solution in anhydrous propylene glycol It has been used satisfactorily in some cases in doses of 6 mg 2 or 3 times a day Not all patients can tolerate the drug and marked bradycardia even epileptiform convulsions have sometimes followed its use Atropine sulfate will abolish such side effects Tolerance to atropine may increase so that 2 to 3 mg every hour are necessary to control side effects Tetra ethylpyrophosphate must be studied further but it shows promise as a valuable agent in the treatment of myasthenia It is cheap has prolonged action and is especially valuable in patients who have become refractory to neostigmine Side effects are similar to those of neostigmine

Corticotropin and cortisone have been tried in myasthenia gravis and some improvement in a small percentage of the cases studied has been seen following their use Unfortunately some patients grow weaker and are made worse when these drugs are used Corticotropin may be tried in doses of 25 mg intramuscularly every 6 hours

Amyotonia Congenita Oppenheim s Disease

Only symptomatic treatment is available The muscles should be maintained in as good condition as possible The patient should be kept ambulant with the day of final restriction to bed postponed as long as possible Every attempt should be made to avoid contractures, by use of exercises and passive motion If deformities have occurred orthopedic operative procedures may be helpful Along with the care given to the muscles all manner of hygienic measures should be carried out, particularly prophylaxis against and treatment of intercurrent infections Such measures as glycine in doses of 10 gm daily or vitamin E have not been proved to be effective Sudden death may occur usually attributed to myocardial insufficiency

somewhat by the use of testosterone propionate in oil in an intra muscular dose of 50 mg 2 or 3 times a week. A lowered metabolism may sometimes be raised satisfactorily with thyroid extract to the betterment of the patient. Cataracts, if they develop, should be extracted.

Myotonia Congenita Thomsen's Disease

Myotonia congenita is considered by some to be an early stage or simply a variation of form of myotonia atrophica. Treatment for myotonia congenita should be the same as that outlined for myotonia atrophica.

Paramyoclonus Multiplex Essential Myoclonia

There is at present no effective treatment for this condition.

Myasthenia Gravis

The considerable variation that occurs from time to time in the active symptomatology of myasthenia gravis makes an evaluation of therapy for it somewhat difficult. Relapses of considerable severity may occur suddenly, and spontaneous remissions do take place.

The treatment of myasthenia gravis concerns itself with two phases (1) the acute attack, and (2) a long-range program.

For the *acute attack* the patient should have bed rest, with tube feeding if deglutition is disturbed, with maintenance of adequate fluid and electrolyte balance and the proper use of neostigmine (Prostigmine). It is preferable to begin therapy with neostigmine (Prostigmine) methylsulfate, 1 2000 solution, 0 5 to 1 0 mg intramuscularly every 2 hours. When swallowing is unimpaired, use 2 of the 15 mg tablets of neostigmine (Prostigmine) bromide every 2 hours by mouth or combine the oral and parenteral dosage by using 30 mg of the bromide tablet orally every 2 hours and the methylsulfate solution parenterally at 6 hour intervals, depending on the severity of the case. In milder forms 15 mg of neostigmine (Prostigmine) bromide by mouth every 3 or 4 hours is often sufficient. When the 15 mg tablet is used, the dosage and intervals between doses should be scaled up or down to meet the requirements of the individual patient. In most cases dosage needs to be increased during an acute infection, when the patient is fatigued or losing sleep, and sometimes during menstruation. During the acute

exercised not to use these drugs for any other reason in patients with myasthenia gravis because of the aggravation of symptoms which results Likewise, local anesthetics and morphine should be used with great care When using neostigmine to improve the symptoms of myasthenia gravis as a diagnostic test, 0 5 mg of the methylsulfate solution intravenously or 1 5 mg intramuscularly may be tried The improvement should be immediate, in a matter of minutes, and reexamination for function should show at least 50 per cent objective improvement Subjective improvement is to be disregarded Atropine sulfate, 0 6 mg should always be at hand to inject subcutaneously when side effects become manifest, but it should not be injected with neostigmine If side effects become pronounced in a diagnostic test with neostigmine, the disease is not myasthenia gravis

Other drugs that have been tried in the past in the treatment of myasthenia gravis have not proven very satisfactory They may be tried alone or used to supplement the use of neostigmine Ephedrine sulfate, in doses of 10 to 30 mg orally 2 or 3 times a day, has been estimated to have 10 to 15 per cent of the effectiveness of neostigmine Acting probably directly on skeletal muscle tonicity, it may cause increased strength Glycine [aminoacetic acid] has been discarded in the treatment of myasthenia gravis Potassium chloride or citrate, to be effective, must be given in almost toxic doses, 4 0 to 6 0 gm 6 times a day Guanidine hydrochloride, in a total daily dose of 20 to 30 mg per kilogram in divided doses, is not consistently effective and readily causes gastro-intestinal symptoms and disagreeable paresthesias around the mouth and at the finger tips

Pyridostigmine (Mestinon), an analogue of neostigmine, gives excellent results and can replace neostigmine Usually a dose of 60 mg for each 15 mg of neostigmine is satisfactory Pyridostigmine causes less stimulation of the gastrointestinal tract, seems to be more slowly absorbed and gives longer action It gives a smoother control of symptoms and untoward reactions are less frequent and less severe Because of its slower absorption it is less desirable in acute situations As with neostigmine, patients should be alerted to toxic effects such as excessive salivation, myosis, fasciculation of voluntary muscles, and increasing weakness A newer compound of considerable interest is ambenonium (Mytelase) chloride, an active anticholinesterase, with a strong anticurare effect, 2 to 3 times more active than neostigmine with toxic effects similar to those of neostigmine and also counteracted by atropine In a small series of cases

Shoulder-hand Syndrome

In this occasional complication which is usually seen following myocardial infarction, cortisone should be tried first in doses of 200 mg the first and second day, and gradually reduced to 50 to 100 mg a day as a maintenance dose In some cases stellate ganglion block may be helpful Stellate ganglion block may also be useful in shoulder hand syndrome following a cerebral vascular accident

BIBLIOGRAPHY

Diseases of the Muscles and Tendons

1 ATKINSON, W J Jr "Treatment of Myasthenia Gravis with Tetraethyl Pyrophosphate," *South Med J*, 1950, XLIII, p 865
2 FORSHAM, P H Present Status of ACTH and Cortisone Therapy,' *Med Clinic No Amer*, September 1951, p 1229
3 GORRELL R L Musculofascial Pain Treatment by Local Injection of Analgesic Drugs," *Jour Amer Med Assoc*, 1950 CXLII, p 557
4 MILLIKAN, C H, and EATON, L M Clinical Evaluation of ACTH and Cortisone in Myasthenia Gravis" *Neurology*, 1951, I p 145
5 TORDA, CLARA and WOLFF H G "Effects of Adrenocorticotrophic Hormone on Neuromuscular Function in Myasthenia Gravis' *Proc Soc Exper Biol and Med*, 1949 CXXI, p 43
6 ZARAFONETIS C J D Clinical Use of Para Aminobenzoic Acid' *Texas State J Med*, 1953 XLIX 666
7 SCWAB R S MARSHALL C K and TIMBERLAKE, W WIN 8077 in Treatment of Myasthenia Gravis *Jour Amer Med Assoc*, 1955 CLVIII 625
8 STEINBROCKER, R NEUSTADT D and LAPIN, L "Shoulder Hand Syndrome,' *Jour Amer Med Assoc*, 1953, CLIII 788

rheumatoid arthritis is subject to spontaneous remissions and relapses and that the earlier treatment is begun particularly in the first year the better the results are likely to be In the most recent concept of rheumatoid arthritis if the pathological physiology can be stopped or even reversed, the pathological anatomical changes need not occur Such may be accomplished only when the disease is treated early and vigorously

General Measures Bed rest is an important part of therapy only as it pertains to the stage of the disease and the symptoms present at the time the patient is seen When there is acute activity with swollen tender joints and fever complete bed rest is imperative but that does not mean complete immobilization from which deforming contractures are bound to result In this stage splints or half shells of plaster of Paris are recommended to obtain the optimum position of the joints they should be used part of the day and certainly during sleep when constractures are most likely to occur

In a more subacute stage bed rest for part of the day is useful but in the absence of fever and other signs of activity the patient should be up and around within the limitations of pain but not to the point of fatigue In the more chronic stages of the disease where joint pains are the only manifestation a rest period during the day plus adequate rest at night on a bed furnished with a firm well supported mattress is usually sufficient

Improved nutrition and general hygiene constitute most important measures of treatment in rheumatoid arthritis Whereas in osteo arthritis it is often important to have the patient lose weight in rheumatoid arthritis weight gain is frequently desirable A high calorie nutritious diet should be instituted Vitamins (vitamins A D and C) should be given freely not for any specific effect on the arthritis but for their nutritional value These should be supplied not only in tablets and capsules but in the diet from large portions of vegetables yellow and green and fruit juices At the same time in patients whose acute disease runs a long and protracted course with the necessity of lengthy immobility gross overweight should be guarded against

General hygienic measures include particular attention to foci of infection Although it is true that occasionally the removal of a focus of infection will appear to cause rather prompt remission in certain cases of rheumatoid arthritis an attack on foci of infection with such expectations is not warranted Rather the approach should be one of removing or controlling any infection in the body in terms of improving the gen

CHAPTER LXXII

DISEASES OF THE JOINTS

In this chapter are considered those afflictions of bones, joints, and muscles commonly thought of under a heading of chronic arthritis, namely rheumatoid arthritis with some of its variants—spondylitis (Marie Strumpell), Still's disease, Felty's syndrome, palindromic rheumatism, psoriatic arthritis (Arthropathia psoriatica), and hypertrophic arthritis (sometimes called osteo arthritis) Also to be considered is post-traumatic arthritis Other arthritides, such as rheumatic fever gout Reiter's syndrome, dengue fever, and arthritis due to specific infection such as gonorrhea, syphilis, tuberculosis and other organisms are discussed under their respective headings Such forms of arthropathy as the joint symptoms that may occur as part of a disease process —typhus fever, pre-tibial fever, big heel, influenza, lupus erythematosus, neoplasm, erythema nodosum, hemophilia, hysteria, ochronosis, poly arteritis nodosum Raynaud's disease and serum sickness—will not be discussed here but will be found under their respective headings

Since there are distinct differences in the treatment of rheumatoid arthritis and its variants and osteo arthritis, the subject will be considered under two principle types (1) rheumatoid arthritis, and (2) osteo-arthritis

Rheumatoid Arthritis

Rheumatoid arthritis as it is usually seen, is a chronic debilitating disease with its chief manifestations in the musculo skeletal system at the same time manifesting important constitutional symptoms such as anemia anorexia loss of weight, and weakness Therefore any outline of treatment must consider the patient as a whole, physically and emotionally, and not simply the alleviation of joint pains It has been well said that the treatment of rheumatoid arthritis requires 'patience equanimity, ingenuity and resourcefulness" Furthermore, in any evaluation of the treatment of this disease it must be kept in mind that

Recent studies have shown that the simultaneous administration of para aminobenzoic acid with salicylates has a renal blocking effect on the urinary excretion of the latter thereby maintaining a prolonged level of salicylates in the blood stream The benzoates in themselves, including para aminobenzoic acid have been found to possess to some degree analgesic antipyretic and antirheumatic activity Such a combination of sodium salicylate 0 3 gm and sodium para aminobenzoic acid 0 3 gm (Pabalate) may be tried in doses of 2 tablets 3 or 4 times a day Often with acute and severe pain present the effectiveness of a para aminobenzoic acid salicylate combination is not as good as comparable doses of sodium salicylate alone The combination has a disadvantage of delayed action requiring 4 to 6 hours for maximum benefit This disadvantage is noticed particularly by the patient who experiencing the most joint pain and stiffness on arising in the morning then takes para aminobenzoic acid salicylate and has little relief before noon Subsequent doses during the day may then keep the patient comfortable If it is desirable to use the combination this disadvantage may be overcome by administering sodium salicylate 0 6 to 1 0 gm on arising for its quicker effect followed every 4 hours through the rest of the day by the *para aminobenzoic acid salicylate mixture (Pabalate)* This combination is not as likely to cause salicylism with nausea vomiting gastric discomfort, tinnitus vertigo and deafness as may follow the salicylates alone

Sodium gentisate is also an effective analgesic with an action similar to that of acetylsalicylic acid It is given in the same manner and dosage as acetylsalicylic acid There is some evidence to support the belief that it gives somewhat less severe side reactions than acetylsalicylic acid when toxic doses are given

Recently a pyrazolidine derivative phenylbutazone (Butazolidin) in *a dose of from 200 to 800 mg daily has been introduced for the relief* of the pain and symptoms of arthritis Unfortunately this drug has dangerous potentialities and while it does prove helpful in patients it is capable of causing serious reactions such as anemia gastric irritation and fluid and electrolyte disturbances It must be used, if at all with great caution and only when adequate facilities are available for repeated blood examinations

The application of *heat* by various means will be very helpful in the treatment of rheumatoid arthritis particularly in the early stages of the disease This should be in the form of dry heat such as water bottle *or heating pads applied to the joints a heat lamp or such measures as*

CHAPTER LXXII

DISEASES OF THE JOINTS

In this chapter are considered those afflictions of bones, joints, and muscles commonly thought of under a heading of chronic arthritis, namely rheumatoid arthritis, with some of its variants–spondylitis (Marie-Strumpell) Still's disease, Felty's syndrome, palindromic rheumatism, psoriatic arthritis (Arthropathia psoriatica), and hypertrophic arthritis (sometimes called osteo arthritis) Also to be considered is post-traumatic arthritis Other arthritides, such as rheumatic fever, gout Reiter's syndrome, dengue fever, and arthritis due to specific infection such as gonorrhea syphilis, tuberculosis, and other organisms, are discussed under their respective headings Such forms of arthropathy as the joint symptoms that may occur as part of a disease process —typhus fever pre tibial fever big heel influenza, lupus erythematosus, neoplasm, erythema nodosum, hemophilia, hysteria, ochronosis, poly arteritis nodosum, Raynaud s disease and serum sickness–will not be discussed here but will be found under their respective headings

Since there are distinct differences in the treatment of rheumatoid arthritis and its variants and osteo arthritis, the subject will be considered under two principle types (1) rheumatoid arthritis, and (2) osteo-arthritis

Rheumatoid Arthritis

Rheumatoid arthritis, as it is usually seen, is a chronic debilitating disease with its chief manifestations in the musculo-skeletal system, at the same time manifesting important constitutional symptoms such as anemia anorexia loss of weight and weakness Therefore any outline of treatment must consider the patient as a whole, physically and emotionally, and not simply the alleviation of joint pains It has been well said that the treatment of rheumatoid arthritis requires patience, equanimity ingenuity and resourcefulness" Furthermore, in any evaluation of the treatment of this disease it must be kept in mind that

of corticotropin, injections or oral tablets may be given once a day with the former and should be given several times a day with the latter, or a longer acting repository form effective in 1 or 2 daily injections (Acthar Gel) should be used

Corticotropin should be given in a dose of 50 mg 3 times a day the first day, then 25 mg 3 or 4 times a day thereafter Often with corticotropin a maintenance level can be maintained by giving 10 or 15 mg 3 or 4 times a day If the repository form (Acthar Gel) is used an intramuscular dose of 80 mg should be given at 12 hour intervals on the first day This is followed by 80 mg once a day with this dose subsequently reduced to 20 or 40 mg if possible

Cortisone should be given in an initial oral dose of 300 mg on the first day in divided doses every 6 to 12 hours The dosage should then be reduced to 200 mg on the second day 100 mg on the third day, followed by 100 to 1 5 mg daily thereafter for 7 to 14 days or until desired results are obtained In protracted cases, 50 to 75 mg of cortisone daily may be given for prolonged periods with little harm resulting

On long continued use potassium chloride 1 0 gm 3 times a day should be given When stopping cortisone, the drug should be reduced gradually supplying corticotropin at the same time for 4 or 5 days Combining steroid hormones and salicylates can be most helpful

The steroid analogues prednisone (Meticorten) and prednisolone (Meticortelone) 3 to 5 times as effective as cortisone or hydrocortisone are proving to be very helpful in the treatment of rheumatoid arthritis when such therapy is indicated The oral dosage for both substances is similar beginning with 20 to 30 mg per day, and as improvement is experienced, the dosage is lessened to a maintenance level of 5 to 15 mg a day There is less tendency for sodium retention and potassium loss Steroid hormones and salicylates given concurrently are excellent but the dose of each should be independently adjusted to the proper needs of the patient Combinations of salicylates and steroids in single tablets interfere with proper adjustment of dose and usually do not give as good results as the individual adjustments Since both the steroids and salicylates can cause ulceration and hemorrhage in the gastrointestinal tract patients using them should be observed carefully and a bland diet with antacids used if the dose is large prolonged or if there are any gastrointestinal symptoms of irritation

eral health of the individual Foci of infection still have a place in medicine but not as a specific in rheumatoid arthritis

The general measures of treatment, therefore, should include proper rest local, general and mental, proper nutrition, relief of pain, proper exercises, removal of definitely infected foci, and correctional physical therapy—in other words, those measures which lead toward restoration of the organism to its optimal physiologic function

Specific Measure of Treatment The various therapeutic agents used in the treatment of rheumatoid arthritis may be divided into two categories (1) measures of proved value, and (2) measures of doubtful value or of no usefulness Treatment measures of proved value include the salicylates, heat, transfusions, possibly the pituitary adrenal hormones and physical and occupational therapy Chrysotherapy would be included by some All of these measures are said to be of proved value because usually they demonstrate some benefit in the majority of patients with rheumatoid arthritis with a minimum of undesirable reaction

The *salicylates* have been used chiefly for the relief of pain and discomfort, yet there is some evidence to suggest a certain specificity of action of them in rheumatoid arthritis, one involving the inhibition or inactivation of the enzyme hyaluronidase, the so called "spreading factor"

The salicylates should be administered preferably by mouth either as enteric-coated tablets of sodium salicylate or as acetylsalicylic acid, 0 3 to 1 0 gm every 3 or 4 hours as necessary Some advise the use of far larger doses Salicylates given intravenously have no added benefit and serious toxic effects can occur They may be given by rectum if the patient cannot take the drug by mouth For many years some have practiced the administration of sodium bicarbonate with the salicylates to lessen their gastric irritation It does lessen the gastric symptoms but at the same time it enhances their excretion and reduces the effective blood level of the salicylates, so the adjunctive use of sodium bicarbonate is not recommended With much better enteric coating of tablets today the added use of sodium bicarbonate becomes unnecessary If the effectiveness of the salicylates alone is not satisfactory codeine sulfate in doses of 15 or 30 mg may be added Morphine should not be given for relief of pain in such a chronic condition as rheumatoid arthritis Some patients like the additional use of methyl salicylate [oil of wintergreen] applied locally to painful joints for its counter-irritating effect on the skin Its use may be helpful

of corticotropin injections or oral tablets may be given once a day with the former and should be given several times a day with the latter, or a longer acting repository form effective in 1 or 2 daily injections (Acthar Gel) *should* be used

Corticotropin should be given in a dose of 50 mg 3 times a day the first day, then 25 mg 3 or 4 times a day thereafter Often with corticotropin a maintenance level can be maintained by giving 10 or 15 mg 3 *or 4 times a day If the repository form (Acthar Gel) is used* an intramuscular dose of 80 mg should be given at 12 hour intervals on the first day This is followed by 80 mg once a day with this dose subsequently reduced to 20 or 40 mg if possible

Cortisone should be given in an initial oral dose of 300 mg on the first day in divided doses every 6 to 12 hours The dosage should then be reduced to 200 mg on the second day 100 mg on the third day, followed by 100 to 125 mg daily thereafter for 7 to 14 days or until desired results are obtained In protracted cases, 50 to 75 mg of cortisone daily may be given for prolonged periods with little harm resulting

On long continued use potassium chloride 1 0 gm 3 times a day should be given When stopping cortisone, the drug should be reduced gradually, supplying corticotropin at the same time for 4 or 5 days Combining steroid hormones and salicylates can be most helpful

The steroid analogues prednisone (Meticorten) and prednisolone (Meticortelone) 3 to 5 times *as effective as cortisone or hydrocortisone* are proving to be very helpful in the treatment of rheumatoid arthritis when such therapy is indicated The oral dosage for both substances is similar beginning with 20 to 30 mg per day and as improvement is experienced the dosage is lessened to a maintenance level of 5 to 15 mg a day There is less tendency for sodium retention and potassium loss Steroid hormones and salicylates given concurrently are excellent but *the dose of each should be* independently adjusted to the proper needs of the patient Combinations of salicylates and steroids in single tablets interfere with proper adjustment of dose and usually do not give as *good results as the individual adjustments Since both the steroids and* salicylates can cause ulceration and hemorrhage in the gastrointestinal tract patients using them should be observed carefully and a bland diet with antacids used *if the dose is large prolonged or if there are any* gastrointestinal symptoms of irritation

Transfusion of whole blood is a very useful adjunct to other forms of treatment whether the anemia is mild or moderately severe The anemia in rheumatoid arthritis responds poorly, if at all to the usual liver and iron therapy In this circumstance whole blood transfusions do more than simply elevate the blood level, they provide for distinct benefit in the active process as well as improve the feeling of well being of the patient Good results are often obtained by giving 250 cc of whole blood once or twice a week for several weeks as indicated If the anemia is severe, the hemoglobin and red cell count should be elevated more rapidly as by a daily transfusion until the desired results are obtained

The *steroid hormones*, cortisone and corticotropin, have introduced a new aspect into the treatment of rheumatoid arthritis. Unfortunately these substances are expensive, have toxic side effects, and are helpful only while they are being given The disease usually recurs and is likely to be more severe following their use For the most part, many rheumatologists are now advising against their use

They do however alter the pathological physiology of rheumatoid arthritis with such temporary striking clinical improvement in many cases when given early in the disease that now they are being used widely in the treatment of this disorder The false sense of cure from them no longer persists, and the knowledge has been gained that small doses are often as effective as larger ones and that small doses can be administered over a longer period of time without the hazard of toxic reactions

Both cortisone and corticotropin have been used with about equal effectiveness in the treatment of rheumatoid arthritis If it is decided to use them, they should be limited to the acute early stage of the disease and then as a supplement to the measures outlined on the preceding pages. Often the relief of pain with these substances is so dramatic that the dosage of salicylates can be reduced or even stopped during their administration Upon the withdrawal of cortisone or corticotropin there may occur a 'rebound phenomenon" with high fever and acute exacerbation of symptoms This when it occurs, should be treated symptomatically

Various schedules of dosage have been applied in rheumatoid arthritis, usually with an initial loading dose, followed by a lower maintenance dose for 10 to 14 or more days A completely satisfactory dosage of these substances in the treatment of rheumatoid arthritis has not been established as yet Since the action of cortisone is longer than that

from change of climate, it seems wisest before home and family are moved, to have the afflicted individual assume a temporary sojourn in a new climate, if enough improvement warrants it then the household may be moved

Deep roentgen therapy is usually of no benefit in the treatment of peripheral joints but has its greatest usefulness in the therapy of rheumatoid spondylitis (Marie-Strumpell) This is discussed later under Rheumatoid Spondylitis

The list of measures that have been tried in such a chronic disease as rheumatoid arthritis and found to be wanting if not actually useless is a long one all of which will not be enumerated here Some of the more prominent ones even recently include vaccines large doses of vitamins (Vitamin D) diet fads sulphur bee venom neostigmine (Prostigmine) the sulfonamides penicillin streptomycin antireticulocytotoxic serum, epinephrine hormones other than cortisone and corticotropin such as pregnenolene 21 acetoxy pregnenolone 17 hydroxy delta 1 pregnenedione testosterone propionate calcium succinate aspirin compounds desoxycorticosterone acetate and vitamin C copper and colonic irrigations

The various vaccines most of them directed against streptococci have been of no value Large doses of vitamin D (Ertron) not only are seldom helpful but may be harmful leading to hypercalcemia and renal failure Vitamin deficiency has not been found to be present regularly in this disease and seems to have no causative effect Neostigmine has been thought by some to be useful in relieving associated muscle spasm but even that effect is questionable The chemotherapeutic and antibiotic agents serve their only useful purpose in rheumatoid arthritis in the treatment of specific infections that may exist with no specific effect on the arthritis as such Epinephrine has been tried of course to stimulate the pituitary adrenal system as a substitute for cortisone or corticotropin with very temporary benefit The other steroid hormones testosterone progesterone pregnenolone have likewise been tried to simulate cortisone action usually without benefit Desoxycorticosterone acetate with vitamin C was hailed enthusiastically at first with subsequently very disappointing results in this country The aspirin calcium succinate compounds are very expensive and no better in relieving pain than aspirin alone In the general health of the individual proper bowel elimination is necessary which may be mediated through cleansing

Transfusion of whole blood is a very useful adjunct to other forms of treatment, whether the anemia is mild or moderately severe The anemia in rheumatoid arthritis responds poorly, if at all, to the usual liver and iron therapy In this circumstance whole blood transfusions do more than simply elevate the blood level, they provide for distinct benefit in the active process as well as improve the feeling of well being of the patient Good results are often obtained by giving 250 cc of whole blood once or twice a week for several weeks as indicated If the anemia is severe, the hemoglobin and red cell count should be elevated more rapidly as by a daily transfusion until the desired results are obtained

The *steroid hormones*, cortisone and corticotropin, have introduced a new aspect into the treatment of rheumatoid arthritis Unfortunately these substances are expensive, have toxic side effects, and are helpful only while they are being given The disease usually recurs and is likely to be more severe following their use For the most part, many rheumatologists are now advising against their use

They do however, alter the pathological physiology of rheumatoid arthritis with such temporary striking clinical improvement in many cases when given early in the disease that now they are being used widely in the treatment of this disorder The false sense of cure from them no longer persists, and the knowledge has been gained that small doses are often as effective as larger ones and that small doses can be administered over a longer period of time without the hazard of toxic reactions

Both cortisone and corticotropin have been used with about equal effectiveness in the treatment of rheumatoid arthritis If it is decided to use them, they should be limited to the acute early stage of the disease and then as a supplement to the measures outlined on the preceding pages Often the relief of pain with these substances is so dramatic that the dosage of salicylates can be reduced or even stopped during their administration Upon the withdrawal of cortisone or corticotropin there may occur a 'rebound phenomenon' with high fever and acute exacerbation of symptoms This, when it occurs should be treated symptomatically

Various schedules of dosage have been applied in rheumatoid arthritis, usually with an initial loading dose, followed by a lower maintenance dose for 10 to 14 or more days A completely satisfactory dosage of these substances in the treatment of rheumatoid arthritis has not been established as yet Since the action of cortisone is longer than that

Reiter's Disease

This is discussed on page 316

RHEUMATOID SPONDYLITIS (MARIE STRUMPELL)

This syndrome is a form of rheumatoid arthritis involving principally the spine and sacro iliac joints Whether the joint involvement is confined to the spine and sacro-iliac joints or involves other peripheral joints, the management should be that of a systemic disease The same measures that have been outlined for rheumatoid arthritis should be instituted with special emphasis on certain features

During the acute stage rest and heat properly applied, are most useful A high calorie high vitamin diet should be maintained Rest should consist of confinement to bed on a firm surface preferably flat with a small pillow under the lumbar spine to maintain normal lordosis In severe cases a body cast of plaster of Paris should be used Deep-breathing exercises should be carried out several times a day to prevent fixation of the thoracic cage Hot moist packs to the back as outlined under the treatment of acute poliomyelitis carried out 3 or 4 times a day are very helpful in relieving pain and muscle spasm Muscle antispasmodics such as mephenesin are useful given as described under myositis The salicylates should be used also for pain either in the form of enteric coated sodium salicylate or acetylsalicylic acid tablets 0 3 to 1 0 gm every 4 to 6 hours as necessary More recently cortisone and corticotropin, given as outlined under rheumatoid arthritis have been found to be most helpful during the acute stages of Marie Strumpell spondylitis

In the subacute phase of this disorder small doses of high voltage roentgen therapy given to the spine at frequent intervals have been found to be a most beneficial form of treatment. These should be supervised by a competent radiologist

In the chronic form of the disease when the spine is rigid from ankylosis of bone and calcification of ligaments therapy may have to be largely symptomatic Some of the manifestations of this stage of the disease may be avoided largely by proper therapy in the early stages as outlined in preceding paragraphs Such analgesics as the salicylates may have to be continued for long periods of time yet as the spine becomes fixed and the disease process burned out often the pains disappear

Intra-Articular Injection of Hydrocortisone

Hydrocortisone acetate (Hydrocortone) has been applied very effectively in the treatment of single joint involvement in rheumatoid arthritis Arthritic peripheral joints, the temporomandibular, acromioclavicular, and sternoclavicular joints may be injected with benefit Because of difficulty of injection, and the hazard of spinal cord injury, injections into joints of the spinal column should only be attempted with great caution

After application of usual aseptic precautions and local anesthesia with 1 per cent procaine, the joint cavity should be entered, usually on the extensor surface where the synovial pouch is closest to the skin Any joint fluid present should be aspirated If the joint fluid is purulent, with evidence of infection in or near the joint, hydrocortisone should not be instilled For the knee, ankle, shoulder, elbow, or wrist joints, a 20-22 gauge needle, 1½ to 2 inches long is quite satisfactory The same sized needle may be used also for an anterior approach to the hip joint For a lateral approach to the hip, a 20 gauge 3 or 3½ inch long needle is better Inject from 5 to 50 mg hydrocortisone acetate into the respective joint, this may be repeated in 4 to 6 days for several injections if necessary No harm is done if the solution is injected outside the joint space, but it is ineffective and the material is wasted The injection treatment of ankylosed joints is valueless

Physical and occupational therapy constitutes a very important part of treatment of rheumatoid arthritis, particularly after the acute manifestations of the disease have subsided and chronic deformities have appeared Certain physical therapeutic measures, such as paraffin or hot sand, casts to prevent deformities, and mild passive exercises to prevent muscle atrophy, should be carried out as early as possible, but active exercises and rehabilitation measures should be left for the quiescent later stages In the more chronic forms of the disease corrective orthopedic measures should be considered, such as manipulation under anesthesia, osteotomy, arthrodesis, synovectomy, and reconstruction operations to improve the functional usefulness of involved joints

Some measures in the management of rheumatoid arthritis, not unanimously accepted, include climate and roentgen therapy A warm, dry climate may be helpful for the comfort of a patient with rheumatoid arthritis, but a change in climate does not necessarily guarantee benefit Change of climate may provoke economic hardship To test out benefit

Osteo Arthritis Hypertrophic, Degenerative Arthritis

In this chronic affliction the general aims of treatment should be directed toward rest of the affected part, the relief of pain, heat and massage, correction of mechanical stress defects and proper psychotherapy During the patient s first visit the doctor should explain carefully that this form of arthritis does not usually lead to severe deformity and crippling *That will do much to allay the fears of rheumatism"* and to obtain the best co operation of the patient

General Measures of Treatment Most of the measures outlined under general measures of treatment for rheumatoid arthritis should be applied to the patient with osteo arthritis Some exceptions or variations that are more applicable to osteo arthritis will be given in the following paragraphs

The principle of rest should be applied both generally and locally In contrast to rheumatoid arthritis the patient with osteo-arthritis does not ordinarily require prolonged bed rest During acute episodes particularly of the spine hip or knee bed rest may be necessary to provide adequate local rest to the affected part In this case there need not be the fear of ankylosis as may result from prolonged immobilization in rheumatoid arthritis The acute local manifestation is usually of much shorter duration with fewer accompanying constitutional symptoms In the subacute and chronic forms it is highly desirable to have the patient take a rest period at some time during the day, be it only an hour or two after the noon luncheon A change in type of occupation may also be necessary to provide a *physiological rest such as transferring* from a job requiring heavy lifting or much walking to a more sedentary one At the same time complete immobility is to be guarded against or much stiffness and discomfort will result Some movement is to be desired

Osteo arthritis tends much more to be localized, now here, now there than is rheumatoid arthritis which usually presents widespread involvement Therefore rest to the affected joint plays a more prominent role When a joint of the lower extremity is involved it may require bed rest or confinement to a wheel chair *to provide local rest but often a firm* bandage to a knee or an ankle will suffice along with limited use of the involved extremity In the case of a shoulder or an elbow a sling applied to the arm may be very helpful Where fingers are predominantly involved occupational use of the hands should be avoided during the

enemata, but colonic irrigations should have no place in the treatment of rheumatoid arthritis

Special Forms of Rheumatoid Arthritis

There are certain forms of arthropathy, generally considered to be variations of rheumatoid arthritis, that have been designated by special names These include Still's disease, Felty's syndrome, palindromic rheumatism, Reiter's disease Marie-Strumpell disease, and psoriatic arthropathy

Still's Disease

In this form of rheumatoid arthritis of childhood, often with associated splenomegaly, hepatomegaly, and hyperplasia of regional lymph nodes, the therapy should be the same as that outlined on preceding pages for rheumatoid arthritis in the adult

Felty's Syndrome

Felty's syndrome represents rheumatoid arthritis with splenomegaly, leukopenia, and sometimes thrombocytopenic purpura in the adult. Careful study should be carried out for any associated condition causing splenomegaly, leukopenia, or thrombocytopenia In such instances splenectomy may be helpful to the patient On the other hand, splenectomy in what is called Felty's syndrome is usually of no benefit The treatment should be the same as that outlined for rheumatoid arthritis on preceding pages

Palindromic Rheumatism

The name palindromic (recurrent) has been given to an oft-repeated type of painful swelling, usually of the small and medium sized joints that leaves no residual deformities The usual treatment for rheumatoid arthritis with rest, salicylates, and so forth may not be very effective Therapy along the lines of allergy has also not been helpful On the other hand a full course of therapy with gold salts, as outlined on preceding pages may be beneficial

with small doses of phenobarbital such as 15 mg 3 or 4 times a day Phenobarbital is also useful in promoting rest at night Muscle antispasmodics are helpful when there is muscle spasm associated with the osteo-arthritis, as is frequently the case, use mephenesin (Tolserol) as recommended for myositis

Local or regional nerve block with 1 or 2 per cent procaine hydrochloride into the surrounding tissues can be very helpful for severe localized joint pain The use of intravenous procaine solution for the treatment of osteo-arthritis is not recommended

It has been pointed out in the section on rheumatoid arthritis that the maximum benefit to be obtained from such steroid hormones as corticotropin and cortisone is seen in acute inflammatory conditions before pathological anatomical changes occur In osteo arthritis where usually permanent pathological changes are present by the time symptoms are manifest, a beneficial effect is therefore not to be expected and experience has shown that corticotropin and cortisone give only transient relief Their use is not recommended except in the presence of an acute process such as an inflamed Heberden s node or with redness and swelling of any joint

Under certain circumstances the use of estrogenic hormone preparations can be very useful in the therapy of osteo arthritis There is no specificity in the use of estrogens for this disease, but since osteo-arthritis and the menopause occur so commonly together, the use of diethylstilbestrol, 1 0 mg daily or ethinyl estradiol (Estinyl) 0 05 mg a day or every other day given for hot flashes and nervous irritability will add greatly to the comfort of the patient

Liver extract 1 0 cc twice weekly and ferrous gluconate 0 3 gm 3 times a day should be given if anemia is found to be present Severe anemia is unusual in this disease and for the mild forms 2 capsules taken at mealtime of combined liver and iron (Ferrated Liver Concentrate) may be given

Other forms of treatment such as sulfur, large doses of vitamin D, and vaccines are of no proved value Similarly treatment with gold salts has not been effective

Other Measures of Treatment As discussed under rheumatoid arthritis the removal of foci of infection, particularly in the teeth tonsils, sinuses prostate and cervix, should not be approached with an idea of specificity but should be done to improve the general health of the individual

Therapy of this disease with gold salts has not shown promise and in the chronic stages cortisone and corticotropin are of no benefit. Some times corrective orthopedic surgery may be necessary where the disease has been neglected and marked deformities have resulted

The treatment for involvement of peripheral joints that may be associated with rheumatoid spondylitis should be the same as outlined previously for rheumatoid arthritis Whereas deep roentgen therapy may be most helpful for spondylitis, usually it is of little benefit for the peripheral joints

Psoriatic Arthropathy

When psoriasis and joint disease occur together, the latter most commonly resembles rheumatoid arthritis Either one may antedate the other For psoriasis to be distinctly causative, the exacerbations and remissions of both should occur together When that is the case, adequate therapy for the psoriasis should cause improvement in the joint manifestations Ordinarily both conditions will require separate treatment

The *psoriasis* should be treated according to its location and severity On the extremities a preparation of 3 gm salicylic acid, 3 gm ammoniated mercury in 90 gm rose water ointment applied vigorously to the patches after the scales have been removed with soap and water will often suffice in mild cases For the scalp an ointment containing 10 per cent ammoniated mercury in rose water should be rubbed in at night and then the hair shampooed in the morning For nails, palms, and soles, deep roentgen therapy, given by a qualified radiologist, is considered best Good results may also be obtained with high voltage roentgen therapy Undecylinic acid, at first welcomed enthusiastically, has already been largely discarded as an effective mode of therapy for psoriasis In the severe intractable cases, the patient should be referred to a competent dermatologist Large doses of vitamin A, given subcutaneously, are sometimes effective in psoriasis and so are worth trying

The *joint involvement*, when symptomatic, should be treated in much the same manner as outlined for the general measures of treatment for rheumatoid arthritis The steroid hormones, cortisone and corticotropin may be helpful in the severe, acute stages of psoriatic arthropathy Gold salts, if used for the arthritic manifestations of psoriasis, should be given with caution lest the already existing skin lesions predispose to further skin reactions from the gold salt.

tion, will ordinarily cause rapid subsidence of symptoms Graded exercises should then be instituted, at first the patient must avoid weight bearing and then progress to a crutch and a cane He should gradually begin to do straight leg raising while sitting on the edge of the bed bicycle exercises while supine, and later stiff-knee walking As a rule arthroplasty of the knee joint should be avoided Often overlooked in the therapy of osteo arthritis of the lower extremities and particularly the knee joint is the proper care and treatment of any varicose veins that may be present.

Deep roentgen therapy is usually of little or no benefit in the treat ment of osteo arthritis It is not so effective in the therapy of spinal localization as it has been found to be in rheumatoid spondylitis Its use is not recommended

The intra articular injections of hydrocortisone acetate can be most helpful in osteoarthritis For its application see under Rheumatoid Arthritis ' page 845

Traumatic Arthritis

In this section are considered those joint phenomena that may follow and persist after local trauma to a joint, including fractures and dislocations which lead to continuous pain limited motion, and sometimes deformity Acute trauma to a joint may cause exacerbation of an acute or latent rheumatoid arthritis but the changes in a joint that may follow acute injury are usually of the osteo arthritic type

The proper treatment of the acute injury will do much to minimize or prevent post traumatic arthritis Treatment should include immobilization of the part rest to the joint and aspiration of synovial effu sion if fluid is present with a pressure bandage applied immediately In the case of fracture or dislocation proper reduction or manipulation must be carried out in an attempt to re establish the normal joint physiology Continued rest should be maintained until all inflammation has subsided for as long as 7 to 14 days if necessary In severe involvement local support in the form of a roller bandage or a plaster splint or cast should be applied Local injections of procaine may be employed effectively for pain In the case of sprain some advise injection of air into the joint particularly the knee joint, to prevent synovial adhesions As soon as inflammation has subsided passive and active motion should be begun and increased gently

acute or subacute stage when there is much pain and stiffness When the feet are affected weight-bearing should be minimized and the patient must wear properly fitting slippers and shoes Very important is the proper correction of postural defects when any of the weight bearing joints are affected, affording further physiological rest to the particular joints

Toward this same end, to reduce unnecessary stress and strain, the adjustment of proper body weight should be carried out Since many patients with osteo arthritis are overweight a reduction regime is indicated The method outlined under the section entitled Obesity should be followed Thyroid extract is definitely indicated and may be very helpful in patients with both osteo-arthritis and myxedema This association is not uncommon Dosage should be determined as in the treatment of myxedema Even in the absence of myxedema small doses of thyroid extract, such as 15 mg once or twice a day, have been found to be beneficial

For the underweight individual with osteo-arthritis, a proper nutritious diet high in calories and vitamins should be instituted There is no proved specific diet for the treatment of hypertrophic arthritis, the aim should be an optimal body weight, with a proper division of protein, carbohydrate, fat, vitamins, and minerals

Specific Measures of Treatment The long list of specific measures heralded from time to time in the treatment of rheumatoid arthritis has not arisen in the treatment of osteo-arthritis

Drug Therapy Having reassured the patient with osteo arthritis that marked crippling and deformity do not usually result with this disease, the doctor should also point out that the arthritic changes cannot be altered Drug therapy therefore should be aimed at making and keeping the patient comfortable Toward this end in osteo arthritis, particularly in the chronic form as it is usually seen, the salicylates still maintain first place for the treatment of pain Either sodium salicylate or acetyl salicylic acid will be effective for the severe and acute attack when given at regular intervals, 0 6 to 1 0 gm every 4 hours by mouth and for the milder forms, 0 3 to 0 6 gm as needed for comfort In the mild to moderate cases preparations combining the salicylates with para-aminobenzoic acid (Pabalate), 1 or 2 tablets every 4 hours, may also be helpful With the enteric coating now applied so frequently to the tablets, it is not necessary to give sodium bicarbonate with the salicylates to allay gastric symptoms Often it is useful to supplement the salicylates

3 BAYLES T B Hypertrophic Arthritis (Degenerative Joint Disease), *Med Clin No Amer*, Sept. 1950 p 1435
4 CAVE, E. F Pain in the Neck and Upper Extremity *Med Clin No Amer* Sept 1950 p 1323
5 FREYBERG R. H Present Status of Gold Therapy for Rheumatoid-Arthritis *Jour Amer Med Assoc*, 1950 CXLIII p 418
6 FREYBERG R H, TRAEGER, C N PATTERSON M SQUIRES W ADAMS C. N and STEVENSON C Problems of Prolonged Cortisone Treatment for Rheumatoid Arthritis *Jour Amer Med Assoc*, 1951 CXLVII p 1538
7 GRAUBARD D J and PETERSON M C Procaine in Management of Arthritis *Jour Amer Med Assoc* 1949 CXLI p 756
8 ROSENBERG E. F Cortisone ACTH and Other Steroid in Rheumatoid Arthritis A Summary of Experience at a Large Clinic *Med Clin No Amer* Jan 1951 p 3
9 SALASSA R M BALLMAN J L and DRY T J Effect of Para aminobenzoic Acid on Metabolism and Excretion of Salicylates *J Lab and Clin Med*, 1948 XXXIII p 1393
10 SMITH R T Treatment of Rheumatoid Arthritis and Other Rheumatic Conditions with Salicylates and Para aminobenzoic Acid Study of 125 Patients *Lancet* 1950 IIX p 192
11 SMYTH C J FREYBERG R H and LAMPE, I Roentgen Therapy for Rheumatoid Arthritis of Spine (Marie-Strumpell Arthritis Spondylitis Rhizomelique) *Jour Amer Med Assoc* 1941 CXVII p 826
12 TALKOV R. H ROPES MARIAN W and BAUER W Value of Enteric coated Aspirin *N E J Med* 1950 CCXLII p 19
13 VIGNOS P J and DORFMAN R I Effect of Large Doses of Progesterone in Rheumatoid Arthritis *Am J Med Sc*, 1951 CCXXII p 29
14 ZARAFONETIS C J D STEIGER W A GINSBURG, I and HEATHER A J Treatment of Rheumatoid Arthritis with P Aminobenzoate and Acetylsalicylic Acid *Arch Int Med* 1953 XCII 04

The isolated joint phenomena of osteo-arthritis have already been mentioned Several of these will be considered

For the *hands or feet* when the involvement is mild with more stiffness than pain, the use of contrast baths is very helpful These consist of alternate immersion of the part in first moderately warm water for 1 minute, then cool water for 1 minute, for a total of 10 minutes 2 or 3 times a day When there is pain as well as stiffness, the paraffin or sand bath, as outlined under rheumatoid arthritis can be very effective For exercising the hands a small rubber ball grasped in the palm and squeezed is very useful There is available a putty-like plastic material with rubbery consistency called bouncing putty (silicone) that some prefer to the rubber ball for finger and hand exercises

For involvement of the *spine*, heat should be applied during the acute phase of pain and stiffness, and a corset support should be worn to relieve muscle spasm Treatment for the cervical spine is best carried out by the use of a Sayre halter and traction with 5-pound weights or with a Thomas collar In the subacute and chronic stages correction of posture and muscle-strengthening exercises should be carried out These consist of flexion, extension, and rotation exercises of the spine, with the patient lying flat on the floor or standing against a wall A soft inner-spring bed mattress should be stiffened with either table leaves or plywood boards placed between the mattress and the springs, or a firm felt mattress should be substituted for the soft one and bed boards inserted between it and the springs for firm support

For more than mild involvement of the *hip*, bed rest is usually required During the acute stage hot fomentations should be applied with leg traction to overcome associated muscle spasm In the subacute and chronic stage the pain often continues to be severe requiring prolonged use of salicylates Even during pain, extension, flexion and rotation exercises carefully graded, should be instituted Weight reduction in the obese plays its greatest part in the treatment of hip joint involvement For properly balanced weight the legs should always be measured from anterior iliac spine to internal malleolus If one leg is found to be shorter than the other the addition of a lift to the heel of the shoe on the shortened side can be of much benefit When degenerative changes in the hip joints produce severe pain that will not respond to the above conservative measures, or if there is marked loss of motion, vitallium mold arthroplasty is indicated and is usually successful

With *knee* involvement a short period of rest, with heat for inflamma

CHAPTER LXXIII

DISEASES OF THE BONES AND CARTILAGES

Clubbing and Hypertrophic Osteo-arthropathy

Clubbing of the fingers and toes and hypertrophic osteo arthropathy are usually secondary to chronic cardiac pulmonary or intestinal disease Rarely does the condition give symptoms even when its development seems rapid requiring more than symptomatic measures Therapy should consist of an attempt to remove the underlying cause when it can be determined Chronic pulmonary conditions that are causative such as emphysema empyema bronchiectasis malignancy and occasionally tuberculosis, may be correctable if treated as outlined under those headings elsewhere in this book if they can be corrected this will cause recession of the arthropathy Certain types of congenital heart disease with obstructed pulmonary blood flow and cyanosis heretofore fatal may now be corrected by surgical operation with the bettering if not actual disappearance of hypertrophic osteo arthropathy In the chronic intestinal form with methemoglobinemia or sulfhemoglobinemia or both present any causative agents such as acetanilide nitrites phenacetin potassium chlorate sulfonal sulfonamides trional or carbon monoxide must be discontinued and constipation should be corrected Then improvement in the clubbing will follow If methemoglobinemia is found present the patient should be given 0 2 to 0 4 gm methylene blue in enteric coated tablets daily for prolonged periods to correct this condition This may lead to recession of clubbed fingers and arthropathy

In the consideration of clubbed fingers attention needs to be called to a familial type in which there is no cyanosis and for which there is no treatment

Paget s Disease Osteitis Deformans

Paget s disease is now understood to be a lesion characterized by initial bone resorption followed by bone formation The treatment

For the arthritic symptoms that persist long after the trauma, the same general measures should be carried out as just outlined for osteo-arthritis Since synovitis is often very prominent after trauma to a joint, synovectomy should be considered in any chronic, troublesome post traumatic arthritis

Intermittent Hydrarthrosis

In intermittent hydrarthrosis in which the knee is most commonly in volved, either unilateral or bilateral, and in which the etiology is usually obscure, the treatment is largely symptomatic If an allergic factor can be found as the cause it should be eliminated Sometimes this is in food, occasionally due to change in temperature such as an allergy to heat or cold In some cases benefit may be obtained by the use of a vasoconstric tor such as ergotamine tartrate Ergotamine tartrate (Gynergen) should be tried orally, 1 0 mg 2 or 3 times a day for several days Its use should not be prolonged because of possible ergotism with gangrene resulting Hot or cold applications, as experience demonstrates, and avoiding weight-bearing with the affected limb, should be tried Usually there is little or no pain but when present it should be treated with sodium salicylate or acetylsalicylic acid, 0 3 to 0 6 gm every 3 or 4 hours If careful study reveals no evidence of underlying joint disease, particu larly rheumatoid arthritis, synovectomy should be considered in oft recurring cases

Protruded Intervertebral Disc Herniation of Nucleus Pulposus

The treatment of protruded intervertebral disc is considered in the section dealing with sciatica, see page 929

BIBLIOGRAPHY

Diseases of the Joints

1 ADAMS, C H, and CECIL R H Gold Therapy in Early Rheuma toid Arthritis *Ann Int Med*, 1950 xxxiii p 163
2 BATTERMAN, R C., KRYLE, L S and DANN S Analgesic Action of Sodium Gentisate *New York State J Med*, 1951, ci p 1152

FRAGILITAS OSSIUM OSTEOGENESIS IMPERFECTA

Fragilitas ossium a hereditary hypoplasia of mesenchyme with brittle bones often blue sclerotics and if the individual lives long enough, otosclerosis is a condition closely akin to osteoporosis There is no known medical treatment effective for the skeletal defect Such preparations as calcium phosphorus vitamin D, strontium lactate, and tricalcium phosphate have all been used without benefit Estrogens and androgens may be of value in helping maintain a positive calcium balance Every care should be taken to avoid fractures When they occur they should be treated as an ordinary fracture, for usually they heal normally Deformity should be avoided by appropriate splints and other orthopedic measures The eyes require no treatment, and there is no known therapy effective for the otosclerosis

OSTEOMALACIA

Osteomalacia is a generalized bone condition in which there is a failure of calcium salts to be deposited in newly prepared osteoid because of one or several causes including deficiency of vitamin D resistance to vitamin D, renal acidosis and idiopathic hypercalcemia and following the removal of a parathyroid tumor Accordingly in the treatment for osteomalacia it must be considered which of these underlying causes are present

Osteomalacia from simple lack of vitamin D is probably rare in this country but abounds in the Orient Its treatment consists of the daily intake of adequate amounts of vitamin D and calcium The patient should be given a quart of milk a day supplemented by 5 0 gm of calcium gluconate or calcium lactate dissolved in water 3 times a day In this more simple form the vitamin D may be supplied as cod liver oil 4 0 to 8 0 cc daily or as viosterol 6 to 8 minims per day by mouth or as calciferol (vitamin D_2) in a dosage of 25 000 to 100 000 units a day When the osteomalacia has improved sufficiently the dosage of vitamin D should be reduced to an amount adequate to maintain a normal blood calcium and alkaline phosphatase level to avoid the development of hypervitaminosis If tetany is present with the hypocalcemia it can be relieved by the use of an acidifying substance such as 10 cc of 30 per cent calcium chloride diluted in water or mixed with syrup or honey and given 3 times a day after meals

urine alkaline Calcium gluconate may be given as a tablet 2 0 to 4 0 gm 4 times a day, or as a powder 1 heaping teaspoonful in milk 3 times a day A formula to be used under such circumstances should consist of 140 gm citric acid and 98 gm sodium citrate dissolved in 1 liter of water, prescribe 50 to 100 cc of this mixture daily by mouth If hypokalemia is a factor which it sometimes is a combination of sodium citrate and potassium citrate should be given Along with these measures for alkalinization should be given large doses of vitamin D (Calciferol), 25,000 to 100 000 units daily to increase calcium absorption from the gastro-intestinal tract

There is a rare form of tubular acidosis different from the type just considered in the preceding paragraph in which excess calcium is also excreted in the urine leading to osteomalacia it is known as the Fanconi syndrome (hyper aminoaciduria) The treatment of it is the same as that outlined for renal acidosis from tubular insufficiency—alkali plus high calcium intake plus vitamin D A very high phosphate intake should be tried also

Still another form of osteomalacia that requires most careful balance studies during treatment is that caused by idiopathic hypercalcuria with out hypercalcemia and without renal acidosis In these cases there is increased calcium excretion often with renal calculus formation and a tendency to severe osteomalacia Many of these cases have or have had staphylococcus pyelonephritis this should be treated vigorously if found to be present The difficulty with treatment of these patients is that the osteomalacia responds nicely to a high calcium high vitamin D regimen but such therapy must be administered with great caution because of its tendency to cause formation of renal calculi Hyaluronidase (Wydase), 150 turbidity reducing units subcutaneously daily may be tried as a renal stone preventive measure

An uncommon variety of osteomalacia occurs sometimes following the removal of a parathyroid tumor when excessive utilization of calcium and phosphorus takes place The purpose of treatment in this case is to keep the calcium in the blood from going into the bones too rapidly This is accomplished by placing the patient on a low phosphorus intake and no milk Calcium should be given in adequate amounts preferably in travenously by slow drip in the form of 100 cc of 10 per cent calcium gluconate or calcium lactate in 1000 cc of 5 per cent glucose Vitamin D or similar agents are of little benefit With such therapy the hypocal cemia and tetany disappear and the serum alkaline phosphatase level falls to normal The therapy must be prolonged

of Paget's disease should be directed toward decreasing the bone resorption Therapy, therefore, should consist of high intakes of calcium and phosphorus and large doses of vitamin D to increase calcium absorption. The diet should be high in calcium and vitamins, with at least 2 glasses of milk or buttermilk a day Some add to this calcium glycerophosphate, 3 teaspoonfuls per day, and sodium citrate, 2 0 gm 3 times a day Hyaluronidase (Wydase), 150 turbidity reducing units subcutaneously daily, may help prevent renal stone formation Vitamin D concentrate should be given in doses of 50,000 units 3 times a week, along with 50 to 100 mg ascorbic acid daily It is hoped by this method of treatment to keep new bone formation ahead of bone resorption For pain high voltage roentgen therapy may give relief, but usually it is temporary

If for any reason the patient with Paget's disease is confined to bed for a lengthy period of time, the regime above needs to be modified, it can cause hypercalcemia, hypercalcuria, metastatic calcifications including renal calculi, and even 'chemical death' For that reason bed rest should be kept at a minimum, and a diet low in calcium and phosphorus with a high fluid intake should be prescribed Milk and vitamin D should be avoided and if there is hypercalcemia, dextrose and saline are given intravenously Following fractures, and particularly orthopedic operations estrogen therapy such as diethylstilbestrol, 1 0 mg daily may be helpful in decreasing calcium excretion Early ambulation is advised For males in whom sterility might be produced, such use of the estrogens should not be instituted Treatment of a fracture in a bone diseased by osteitis deformans should be the same as for any fracture It heals normally but calcium deposition in the callus may be delayed

In Paget's disease the parathyroid glands should never be removed and parathyroid extract and any acid salts should not be administered

Sometimes osteogenic sarcoma develops in an area of bone involved by Paget's disease This should be watched for carefully and suspicious lesions treated promptly

Leontiasis Ossea

Leontiasis ossea is considered by some to be a form of Paget's disease localized to the skull, yet the condition is characterized largely by new bone formation The treatment should consist of surgical procedures to relieve pressure, severe headache being a common symptom

seminated osteitis fibrosa, areas of brown cutaneous pigmentation, and true sexual and somatic precocity in females but not in males, there is no known effective treatment at the present time other than orthopedic therapy for the skeletal deformities and for fractures as they occur Usually the fractures heal well except those at the upper ends of the femora which have a tendency to bow Such incomplete union results in pseudo arthrosis Orthopedic measures which do not restore weight bearing lines are useless because of the lack of rigidity of the bone

Osteoporosis

Osteoporosis is primarily a disorder of tissue metabolism in which bone resorption continues unabated while bone formation practically ceases Calcium and phosphorus metabolism is only a secondary factor The etiological factors are several either singly or combined and attention should be paid to them in the treatment of this disorder Since the serum calcium phosphorus and alkaline phosphatase levels are normal large doses of calcium and vitamin D are not usually required

The most common form of osteoporosis is seen in the post menopausal state of women under 65 It does occur in men also In this type there is deficiency of estrogen which is the most important factor in treatment Studies have shown that combined estrogen and androgen therapy along with adequate protein in the diet to build bone matrix and adequate physical activity (avoiding immobility) produce the best results The use of estradiol (Ovocyclin) benzoate, ethinyl estradiol (Estinyl) water soluble estrogenic substance (Premarin) and diethylstilbestrol has been advised Estradiol benzoate (Solution Ovocyclin Benzoate in oil) should be given in doses of 1 66 mg every 3 days to 3 3 mg daily when intramuscular therapy is indicated Ethinyl estradiol (Estinyl) 0 05 mg 3 times a day water soluble estrogenic substances (Premarin) 1 25 mg 3 times a day or diethylstilbestrol 1 0 to 1 5 mg daily should be given when oral medication is desired The naturally occurring hormones are usually more satisfactory Hormone therapy should be given for 4 weeks and then skipped for a week Androgen therapy is helpful and may be given in the form of either testosterone propionate or methyl testosterone Testosterone propionate should be given in doses of 25 mg daily to 25 mg every other day intramuscularly methyl testosterone should be used in doses of 40 to 100 mg daily by mouth Smaller doses of estrogens or androgens are often just as effective as larger ones A parenteral

Considerably more common in this country is a condition that has been termed resistance to vitamin D with resulting osteomalacia, for which the patient may require from 150,000 to 600,000 units of vitamin D daily to lessen the fecal excretion of calcium, restore calcium balance in the body and to promote proper bone formation With high vitamin D resistance the patient should be given calciferol (vitamin D), 300,000 to 600 000 units daily by mouth, careful observations of the blood levels of calcium, phophorus, and alkaline phosphatase and the Sulkowitch test for the urinary excretion of calcium must be made daily until a normal balance is reached Although cod liver oil is ordinarily a good source of vitamin D, its use in this form of osteomalacia is usually ineffectual These patients should be given a diet rich in calcium and phosphorus including one quart of milk a day and cheese, turnip greens, eggs, nuts, dates whole soy beans, and cane molasses

Also quite common as a cause of osteomalacia is hypovitaminosis D secondary to steatorrhea with or without diarrhea This may be due to non tropical sprue chronic pancreatitis, or insufficiency of the small intestine The therapy for this type of improper calcium and vitamin absorption is the administration of crude liver extract or folic acid, as outlined under the treatment of non tropical sprue, a low fat diet, and large amounts of the fat-soluble vitamins K, A, D, and possibly E between meals Vitamin K should be administered as menadione, 2 mg daily If proper absorption in the intestine does not occur vitamin K should be given as menadione bisulfite, 1 0 cc (2 mg) subcutaneously, intramuscularly, or intravenously daily Vitamin A should be given in capsules of 25,000 units each 3 to 4 times a day by mouth Vitamin D (Calciferol), 25,000 to 100,000 units daily, should be given, and vitamin E should be administered as alpha tocopherol 25 mg 3 times a day In treating steatorrhea that is causing osteomalacia, it is important to give all 4 of the above vitamins

Another important cause of osteomalacia is renal acidosis from tubular insufficiency with loss of urinary calcium and secondary para thyroid hyperplasia and sometimes nephrocalcinosis and nephrolithiasis. The initial disturbance is a shortage of base treatment requires the ad ministration of base best in the form of a salt of a mineral base with an organic acid, such as sodium citrate sodium lactate or calcium gluconate Sodium citrate should be given in doses of 1 0 to 2 0 gm every 3 or 4 hours by mouth with plenty of water to lessen gastric distress If sodium lactate is prescribed it should be given as a one sixth molar solution 500 cc intravenously 2 or 3 times a day—sufficient to keep the

spinach along with 0.15 gm ascorbic acid 3 times a day for 10 days, then 0.15 gm daily as a maintenance dose

Osteoporosis may be seen also with hyperthyroidism and with inadequately controlled diabetes mellitus In both of these conditions the cause of the osteoporosis is probably a combination of malnutrition mobilization loss of calcium and a lack of vitamin C Primary consideration in treatment should be given to the underlying condition as discussed under Hyperthyroidism and Diabetes Mellitus For the osteoporosis the diet should contain adequate amounts of protein vitamin C sex hormones if indicated and adequate calcium and phosphorus

The *osteoporosis associated with Cushing's syndrome acromegaly* and with the adaptation syndrome (Selye) is less well understood in its pathological physiology The osteoporosis of Cushing's syndrome is helped materially by the administration of androgens Estrogens are less effective Testosterone propionate or methyl testosterone should be given as outlined in the preceding paragraphs on postmenopausal osteoporosis

As in Cushing's syndrome the osteoporosis associated with acromegaly is benefited also by the additional use of androgens given as outlined for post menopausal osteoporosis

In the osteoporosis following injury (Selye phenomenon) the two main factors at work are immobility and decreased food intake The treatment in this circumstance should emphasize for the osteoporosis the intake of a nourishing diet high in protein and vitamins particularly vitamin C, and adequate calcium and phosphorus followed by early ambulation and rehabilitation

There is still a type of *osteoporosis in which none of the etiological factors above can be determined to be causative* which is spoken of as idiopathic osteoporosis The treatment of it should include a nutritious high protein high vitamin diet with adequate calcium and phosphorus and the administration of small doses of both male and female sex hormones as outlined for post menopausal osteoporosis In addition these patients should be given human serum albumin intravenously 5 gm in 25 cc solution daily this may aid bone matrix formation At best idiopathic osteoporosis does not usually respond to treatment as well as the other types outlined in preceding paragraphs

Multiple Myeloma

Multiple myeloma is a neoplastic like growth involving the skeleton

Achondroplasia Chondrodystrophia Fetalis

For this form of dwarfism there is no specific treatment Usually easy to differentiate from other forms of dwarfism, achondroplasia has no associated mental, sexual, or other endocrine disturbance, so endocrine therapy is of no benefit Sometimes orthopedic surgical procedures may be used to correct unusual deformities

Dyschondroplasia Multiple Cartilagenous Exostoses

In dyschondroplasia there occur irregular juxta epiphyseal hyper ostoses, chiefly of the hips, knees, ankles, shoulders, and wrists When these are large enough to cause pressure on nerves or blood vessels with symptoms they should be removed by surgical excision

Oxycephaly Steeplehead

In oxycephaly there is premature closure of sutures with resulting headaches, exophthalmos and optic atrophy For any of these complica tions or for cosmetic reasons, the only treatment is cranial decompression

Cleidocranial Dysostosis

For this peculiar anomaly of development with its large skull prom inent cranial bones, and defective clavicles there is no definitive treatment

Hyperostosis Frontalis Interna Metabolic Craniopathy

For the bony overgrowth of the inner table of the skull there is no specific therapy Most patients need no treatment for the bone lesion Obviously surgical removal is out of the question Surgical decom pression of the skull however, may be helpful for headache Pituitary irradiation has also been advised to relieve head pains when present High-voltage x ray treatment to the bony exostoses, however, is of no benefit

Associated conditions especially the neurological ones, which are probably not directly related to the disease should be treated sympto matically

Polyostotic Fibrous Dysplasia Ostitis Fibrosa Disseminata Albright's Syndrome

For this peculiar metabolic disorder of bone characterized by dis-

be necessary for pain and discomfort Corticotropin may be helpful to some patients but the results do not last It should be given as described for Rheumatoid Arthritis

MISCELLANEOUS AFFECTIONS OF BONES AND CARTILAGES

Marble Bone Disease Osteopetrosis Albers Schonberg s Disease, Osteosclerosis

In this metabolic bone disease there is too little bone resorption with resulting marked density of all the bones the bones come to resemble marble For the bone condition there is no known treatment Associated features such as anemia should be treated with liver and iron as described under Anemia although refractoriness to therapy may be encountered since the anemia is often due to diminution of the medullary spaces There is no effective therapy for the enlarged liver and spleen that may occur Fractures should be treated adequately by appropriate surgical means and deformities corrected by orthopedic measures Calcium phosphorus cod liver oil vitamin D and any drugs that promote calcification of bone should be avoided Childbearing is contraindicated

Spondylolisthesis

Mild forms of spondylolisthesis particularly when asymptomatic may require no treatment With pain and discomfort which is usual a well fitting corset or steel brace to the back may suffice In the more severe forms with marked subluxation continued pain and sometimes motor and sensory paralysis a bone fusion operation should be performed If untreated secondary arthritic changes develop which may lead to increasing disability In the treatment of low back pain careful consideration should be given to the possibility of a ruptured intervertebral disc causing the pain or co existing with spondylolisthesis lest the latter be operated for without being the full cause of the disability

Compression Fractures of the Spine

In the early stage compression fractures of the spine should be treated by proper immobilization and if spinal cord involvement is present treated as outlined for acute injuries of the spinal cord In the late stage if there is no pain and no neurological involvement no treatment is

preparation containing testosterone propionate with estrogenic substances is available for convenient dosage A dose of 1 to cc 2 or 3 times a week intramuscularly is usually satisfactory, but for best results the dose must be adjusted to the needs of the patient

Water soluble estrogenic substances (Premarin), combined with methyltestosterone in single tablets containing 0 625 to 1 25 mg of the former and 5 to 10 mg of the latter which can be given by mouth make administration much easier The dose is adjusted to the patient s needs The treatment must be prolonged for months to years Progesterone is of no effectiveness in post-menopausal and senile osteoporosis. The osteoporosis that may result from estrogen lack from other causes such as ovarian agenesis, panhyopituitarism, and, in certain instances, from lack of pituitary gonadotropic hormone should be treated as outlined in the preceding paragraph

If edema develops under sex-hormone therapy the sodium intake in the diet should be reduced Further, ammonium chloride should be used in doses of 1 0 gm 3 times a day supplemented with the use of mercurial diuretics If the edema persists, the estrogenic hormones should be reduced in dosage Excess calcium and vitamin D are to be avoided since hypercalcuria with nephrolithiasis may result An accompanying urinary tract infection should be treated with the proper antibiotics

In old age the atrophy of tissues includes bone with the changes of osteoporosis spoken of as senile osteoporosis The treatment should be the same as considered in the preceding paragraph under post menopausal osteoporosis with particular emphasis on adequate physical activity, and a diet high in protein and vitamins so often lacking as a result of the whims of the elderly

Osteoporosis occurring from the atrophy of disuse should be treated by early ambulation and rehabilitation when possible A diet high in protein is of paramount importance Sex-hormone therapy is not indicated unless the patient is past the menopause, or unless there is evidence of lack of sex hormones in the body

The osteoporosis following malnutrition should be treated primarily with a nutritious diet high in protein calcium, phosphorus and vitamin D The minerals tend to decrease the amount of bone resorption but do not stimulate osteoblastic activity

Osteoporosis may be seen with adult scurvy (hypovitaminosis C) usually with malnutrition and sometimes in association with hyperthyroidism In addition to a high protein diet the patient should be given food rich in vitamin C, such as citrus fruits tomato juice, cabbage and

for which sodium salicylate or acetylsalicylic acid in doses of 0 3 to 0 6 gm should be used Constitutional symptoms are absent

Melorheostosis Flowing Hyperostosis

Melorheostosis is a very rare condition characterized by irregular overgrowth of the cortex of bone resembling drippings of a wax candle There is no effective treatment for the condition

Solitary or Eosinophilic Granuloma

Eosinophilic granulomata are solitary destructive tumors of bones histologically related to Hand Schuller Christian s disease The lesions are benign and radiosensitive After proper diagnosis is made by biopsy the lesions should be excised if small and singular or treated by high voltage roentgen rays Corticotropin 25 to 75 mg daily or cortisone 100 to 200 mg daily may be tried

BIBLIOGRAPHY

Diseases of the Bone and Cartilage

1 ALBRIGHT F and REIFENSTEIN E C Jr *Parathyroid Glands and Metabolic Bone Disease* William and Wilkins Co Baltimore 1948
2 FINCH C A Methemoglobinemia and Sulfhemoglobinemia *N E J Med* 1948 ccxxxix p 470
3 HARRINGTON W J and MALONEY W C Treatment of Multiple Myeloma with Urethane *Cancer* 1950 iii p 253
4 KNIES P T and LEFEVER N E Metabolic Craniopathy Hyperostosis Frontalis Interna *Ann Int Med* 1941 xiv 1858
5 LOGE J P and RUNDLES R W Urethane Therapy in Multiple Myeloma *Blood* 1949 iv p 01
6 THORN G W FORSHAM P H FRAWLEY T F HILL S R ROCHE M STAEHELIN D and WILSON D L Clinical Usefulness of ACTH and Cortisone *N E J Med* 1950 ccxxxxii pp 783 824 865

lymph nodes, and sometimes the liver, and is usually fatal in 1 to 2 years. Spontaneous remissions with longer life do occur, however

The treatment for multiple myeloma is high-voltage roentgen therapy administered by a competent radiologist X-ray is most useful for relief of back pain, which may be severe and intractable Stilbamidine and pentamidine have been suggested for the treatment of multiple myeloma. Neither of them has any effect on the ultimate outcome of the disease, but they may cause temporary symptomatic improvement Either drug may be tried in courses of 15 to 21 daily intramuscular or intravenous injections The recommended dosage for stilbamidine is 50 mg the first day, 100 mg the second day, 150 mg the third day, and 150 mg daily thereafter For intravenous injection the stilbamidine should be dissolved in 10 cc of water, for intramuscular injection it should be dissolved in 5 cc of 2 per cent procaine hydrochloride If no albuminuria is present this dosage should be given daily With albuminuria it is advisable to give the drug every other day, or only twice a week, because of its nephrotoxic effect Pentamidine may be used in the same manner as outlined for stilbamidine With either drug atropine sulfate 0.4 mg should be given hypodermically 30 minutes before each injection to minimize vasomotor reactions For the greatest effectiveness of these drugs it is advisable to give, at the same time, a diet low in protein, less than 70 gm a day, since animal protein appears to oppose the action of stilbamidine Careful assessment of renal function before and during diamidine therapy should be made In view of the serious toxic effects these drugs are being abandoned, since good results are seldom observed after their use

Sometimes temporary benefit may be obtained in multiple myeloma by the use of ethyl carbamate (urethane), beginning with 1 0 gm by mouth the first day, 2 0 gm the second day, and 3 0 gm the third day, and maintaining the dose at 3 0 to 6 0 gm daily, for as much as a total of 150 to 240 gm A second course of therapy can be given if necessary Urethane may cause nausea and vomiting

Orthopedic appliances by removing pressure from compressed vertebrae may be very helpful When the anemia becomes severe the patient should be given repeated transfusions of whole blood Anti anemic therapy with liver and iron are totally ineffective If thrombocytopenic purpura occurs splenectomy is indicated for this part of the condition. The involved bones are susceptible to fracture, and therefore the patient should be cautioned against physical trauma Adequate rest and nourishment are important in treatment and further symptomatic measures may

PART XXI

DISEASES OF THE NERVOUS SYSTEM

CHAPTER LXXIV

FUNCTIONAL DISEASES OF THE NERVOUS SYSTEM

Functional diseases of the nervous system constitute one of the most important fields of medicine The frequency of the disease the variety and complexity of the syndromes presented and the skill and time required for treatment have all contributed toward making this field a serious problem to the medical profession Unfortunately all too frequently these patients are neglected or mishandled by the busy physician who has neither the time inclination nor training to diagnose and treat them successfully Since many of these patients can be given great relief and be returned to an adjusted useful productive existence through intelligent management it is essential that physicians recognize the disease and employ proper therapy

For therapeutic purposes functional diseases may be separated into two general categories—the psychoneuroses and the psychoses The relatively benign psychoneuroses consisting of anxiety neuroses compulsion neuroses hysteria the milder depressive reactions and neurasthenia are of common occurrence and for the most part represent no serious mental derangement Frequently they are relieved by proper therapy The psychoses consisting of schizophrenias paranoia manic depressive psychoses involutional psychoses presenile arteriosclerotic and senile psychoses represent serious functional disorders exhibited by a mind so disturbed as to confuse reality with fantasy In general these disorders present difficult therapeutic problems and require specialized skill for their management

required When such symptoms are present proper spinal fusion should be done

Morquio's Disease

There is no known effective treatment for this familial dwarfism resembling achondroplasia Orthopedic measures such as osteotomy may be indicated to lessen functional disability

Gargoylism Hurler's Disease

No effective prophylaxis or treatment is known for gargoylism Most cases die early of intercurrent infections Unlike cretinism, it is not benefited by thyroid extract

Hereditary Arthrodysplasia and Dystrophy of the Nails

In this condition there are developmental defects in certain joints, particularly the knees, elbows, and shoulders, as well as dystrophy of the nails of both fingers and toes There is no effective treatment known, but for impaired joint function orthopedic measures may be necessary

Arachnodactyly

Since subjective symptoms are usually few or absent, therapy should be directed toward special training in the use of deformed structures such as the hands If much deformity of the feet exists, orthopedic measures should be instituted to insure proper walking

Hypertelorism

There is no therapy effective in the prophylaxis or cure of hypertelorism If mental deficiency has not occurred and visual defects are present, the aid of an ophthalmologist should be sought Sometimes there is an associated torticollis, which should receive proper treatment.

Basilar Invagination of the Skull Platybasia

This condition is considered elsewhere (see p 862)

Tietze s Disease Non suppurative Non specific Swellings of Rib Cartilage

In this peculiar affliction of unknown etiology the condition is self limited and usually requires no treatment There may be localized pain,

PART XXI

DISEASES OF THE NERVOUS SYSTEM

CHAPTER LXXIV

FUNCTIONAL DISEASES OF THE NERVOUS SYSTEM

Functional diseases of the nervous system constitute one of the most important fields of medicine The frequency of the disease the variety and complexity of the syndromes presented and the skill and time required for treatment have all contributed toward making this field a serious problem to the medical profession Unfortunately all too frequently these patients are neglected or mishandled by the busy physician who has neither the time inclination, nor training to diagnose and treat them successfully Since many of these patients can be given great relief and be returned to an adjusted useful productive existence through intelligent management it is essential that physicians recognize the disease and employ proper therapy

For therapeutic purposes functional diseases may be separated into two general categories—the psychoneuroses and the psychoses The relatively benign psychoneuroses consisting of anxiety neuroses compulsion neuroses hysteria the milder depressive reactions and neurasthenia are of common occurrence and for the most part represent no serious mental derangement Frequently they are relieved by proper therapy The psychoses consisting of schizophrenias paranoia manic depressive psychoses involutional psychoses presenile arteriosclerotic and senile psychoses represent serious functional disorders exhibited by a mind so disturbed as to confuse reality with fantasy In general these disorders present difficult therapeutic problems and require specialized skill for their management

too much coffee tobacco or alcohol lack of sleep needless emotional turmoil and inadequate relaxation and recreation must be remedied at once A nutritious high vitamin diet eaten slowly under pleasant circumstances is desirable If the patient is underweight a definite attempt should be made to have him gain weight Weir Mitchell who was very successful in treating these patients observed many years ago that frequently they are helped by a gain in weight Regular hours of sleep and relaxation should be established *It is most desirable for the patient* suffering from the exhaustion produced by an anxiety state to receive extra rest Frequently 9 or 10 hours of sleep at night augmented by relaxation and when possible sleep during the middle of the day is necessary Long rests on the week ends are desirable for the working *person Rising late in the morning and after dinner naps on Saturday and* Sunday frequently do much to strengthen a tired exhausted mind

Relaxation should be pleasant and arranged to avoid stress or strain Reading is usually excellent providing the material is simple interesting and of the type enjoyed by the patient Properly selected motion pictures or television programs are relaxing to some individuals and do much to smooth and relax them Conversation can be useful provided it is properly regulated and is desired by the patient

A long vacation arranged to avoid the noise of cities excitement crowds stress of social engagements and strenuous physical activities is occasionally required for the patient to gain back needed strength

Care must be taken to prevent the patient from developing into an invalid who feels that any exertion is bad He must be urged to keep active in useful productive work that gives him a sense of accomplishment

Psychotherapy Unless the physician has the personality time and inclination to institute proper psychotherapy it is wise to refer the patient to a psychiatrist or to one who is capable of applying corrective measures In the hands of the skilled physician psychotherapy has much to offer and it is a most effective tool in the treatment of these patients The physician must first consider the patient as a whole rather than as a diseased lung kidney or heart He must think of his patient as a human being and realize that the symptoms presented are the reaction of the organism as a whole to a noxious stimulus in this case mental tension

The first step is to get thoroughly acquainted with the patient and fully informed about his heredity and development to understand the type of person he is and learn his reactions to the usual stresses of life

Psychoneuroses

The treatment of mental disease in this category commences with a thorough, carefully taken history during which the physician exhibits a sympathetic encouraging, benevolent attitude He should be unhurried and make every effort to secure as close a physician patient relationship as possible This is followed by a thorough physical examination and such laboratory work as needed to orient the physician Care must be taken to avoid alarming the patient during any phase of the history or examination The physician must maintain a calm interested attitude He must use care not to arouse suspicion by too prolonged an examination of any particular organ or area A friendly smile and a reassuring attitude are important Studies should be continued until an accurate diagnosis is made if that is at all possible At the end of the examination the physician should explain to the patient in a calm, authoritative, and sympathetic manner that there is no organic basis for his symptoms He must explain then that the symptoms are produced by functional disease and that a definitely organized plan of treatment is necessary At this point it is essential that the physician explain in simple terms the importance of functional disease the factors that can cause, modify, or relieve it The patient should be reassured that with proper treatment he will secure relief but that much will depend on his own efforts as guided by the physician It is recommended that whenever possible the physician seek the advice of a psychiatrist, since improper diagnosis and treatment may cause considerable damage Unfortunately only a small percentage of these patients can be seen by a trained psychiatrist, and therefore it is necessary for the physician to understand their problems and apply effective measures of treatment while at the same time exercising great care to avoid causing injury

The patient should be seen frequently and from the beginning a regular schedule of visits should be established The vast majority exhibit anxiety and it is this tension which the physician must endeavor first to relieve Treatment consists of general measures for rehabilitation psychotherapy supplementary measures usually of temporary value and special technical procedures employed by the specially trained physician

General Measures A carefully designed program of physical and mental rehabilitation should be commenced immediately Many of these patients are suffering from emotional mental, or physical strain caused by easily correctible factors Excessive hours of work poor nourishment

Environmental manipulation although very helpful at times, is generally most successful where unusual environmental stress of a temporary nature exists Disturbing environmental conditions serve to bring out more rapidly the underlying personality stress and conflicts and these of course are not relieved when the environmental factor is removed

Many patients however cannot be helped by environmental manipulation and in those cases where some environmental changes can be made there may still remain considerable emotional tension or inability to adjust and enjoy equanimity of mind It is therefore necessary *to strengthen the individual so that he can cope with his situation* more adequately It is far better to develop the patient s ability to meet stressing environmental problems with confidence and freedom from anxiety than to remove stress by manipulating the environment artificially *even in cases where this is possible*

In order to develop this ability to adjust to his problems the patient must usually experience or be subjected to the following essential procedures. First he should be encouraged to release his emotional tension by talking over his problems with the physician The opportunity thus offered to get it off his chest frequently proves most helpful The statement and explanation of his difficulties to another person not infrequently help him to decide on a course of action that leads to a release of his tension The physician must encourage the patient to talk and must be sympathetic in his attitude but he should not make the patient s decisions for him As the patient s problems unfold he may recognize the relationship between his symptoms and his mental state If not *this relationship should be pointed out to him by the physician* Following the verbal carthursis the physician employs explanation

Explanation consists of the physician s explaining the nature of the difficulty *the meaning of functional alteration* as contrasted to organic damage the great variety of symptoms their relationship to family (the influence of a nervous emotionally unstable parent on a growing child) home (insecurity produced in the mind of a child by broken unstable home) mental hygiene of the growing child (uncontrolled emotion poor mental habits lack of reasonable mental discipline) and conflict in economic social marital sexual and religious activities

Reassurance should follow explanation It should be sincere, authoritative and optimistic but care must be taken to avoid too glib promises. In general the physician should point out the frequency of functional diseases how they may occur in any *individual if sufficient stress is*

The history carefully taken opens the door, and from this beginning a more complete understanding and appreciation of the patient, his problems, and how he reacts to stress may be developed

In order for the physician to secure proper insight, the patient's entire life must be developed from the beginning in a detailed chronological fashion The familial social, religious, sexual, marital, occupational, and financial spheres must all be thoroughly explored, and areas where stress has occurred or is occurring should be noted The patient must be encouraged to talk about himself, and the physician must be a sympathetic listener who makes every effort to build up the patient's confidence in the authority, wisdom, and understanding of his physician Excellent rapport is often the key to successful psychotherapy

As the relationship and understanding develop, the physician should urge the patient to think more and more of causes and steer him away from symptoms, but the doctor must not interject his own personality or interfere with the free, complete, and spontaneous expressions of the thoughts, problems, and needs of the patient From the beginning to the end the physician must maintain the role of a sympathetic and interested listener

As knowledge of the patient is gained, the physician will often begin to see where there is a relationship between the patient's symptoms and stress in one or more of the previously mentioned spheres of influence Once this conflict is recognized, the physician must decide what is the best way for the patient to handle the situation Usually after any physical abnormality or poor habit is corrected, only two courses are available The environment may be altered so as to eliminate undesirable stressing influences or the patient may be strengthened by therapy that will enable him to cope with any strain created by environment or his mental condition

Not infrequently it is possible to alter certain unnecessarily stressing environmental situations and whenever possible, this should be done A friendly talk with the patient's family, wife, or employer can on occasions accomplish more toward the relief of indigestion than pounds of antacid powder At this stage a skilled social worker, through development of knowledge and understanding of the patient's social and economic adjustment, often proves extremely helpful in guiding the physician Furthermore the assistance of such trained workers in helping the patient adjust to his environment is often invaluable, since frequently they can cross barriers and settle difficulties that might never be attempted by the patient

from their tension by going to church, developing a useful hobby or joining a group working on a project that is both interesting and stimulating to them The sense of accomplishment obtained by helping some less fortunate neighbor is excellent for these patients, since it bolsters their self confidence and strengthens their desire to conquer their difficulties

Finally, the patient should be toughened mentally in order to face his own problems As his confidence grows he should make use of every opportunity to face and overcome situations that cause him tension or prevent him from enjoying a normal existence He must progress from the simpler and more readily controlled situations to the more difficult and complex Each success leads to greater strength

Supplementary Measures Other forms of therapy are occasionally of value as supplementary procedures In general however they are of temporary use and must be employed in conjunction with psychotherapy if good results are to be obtained

The sedatives are helpful for temporary relief, especially if there is a temporary unusual strain Phenobarbital 15 mg 4 times a day proves soothing to many individuals If acute insomnia is causing considerable concern to the patient a hypnotic dose of 0 1 gm of phenobarbital at bedtime is recommended Chloral hydrate in a 0 5 to 1 0 gm dose at bedtime is a useful preparation possibly better than phenobarbital as it acts promptly and produces sleep with very little residual effect It is unwise to continue sedation for a longer period than 10 days to 2 weeks and care must be taken to limit the amount of drug prescribed so that the patient cannot continue on the sedative longer than the period recommended

Several recently introduced drugs are very useful in the treatment of both psychoneuroses and psychoses These are Rauwolfia serpentina and its derivatives or chlorpromazine azacyclonol, and meprobamate Reserpine (Serpasil) one of the active principals of Rauwolfia serpentina may be tried in doses of 0 25 mg, at first 2, then 3 times a day In psychoses it may be given from 6 to 18 mg daily Chlorpromazine (Thorazine) 25 to 50 mg 4 to 6 times a day can be very effective Larger doses are occasionally necessary therefore it is wise to increase the dose slowly to meet the patient s needs or until minor toxic effects appear As much as 2 5 gms have been given daily Usually, however a dose of 0 8 gm or less a day is satisfactory It should be remembered that chlorpromazine potentiates other sedatives that may be being given

brought to bear, the lack of dangerous organic impairment, and the reasonable probability of relief provided proper treatment is carried out Frequently it is necessary to reassure the patient repeatedly, but the physician must make certain each time that he does not promise too much and must emphasize that progress depends on the patient's efforts to control his malady In other words, the patient must share the responsibility of his own recovery Not infrequently it is necessary to convince the patient that he wants to, and must, get well, since some individuals have found that their symptoms serve a useful purpose, such as avoidance of work, avoidance of facing unpleasant situations, getting desired attention from family and friends, and obtaining insurance compensation or pensions and other normally unattainable recognition In order to overcome this, the physician must use persuasion and must encourage the development of confidence and the desire to face and conquer the problem

Suggestion is a useful tool and can be employed to advantage as proper situations develop The physician must consider this as a temporary therapeutic measure to be used as a means of establishing confidence and encouraging the patient to take steps necessary in his treatment

As the physician gains knowledge of his patient, he will realize that much of the tension created is the result of the patient's lack of information about the normal functioning of the mind and body Incorrect information, half-truths badly distorted ideas and information, either correct or incorrect, which are bound up with unfortunate emotional material frequently can be found to be the source of tension For example, the anxiety that may appear when a patient fears he has a cancer may be severe enough to produce symptoms, but once the patient is convinced by the doctor that he does not have this disease, his symptoms and anxiety disappear Therefore, it is necessary to undertake a program of explanation, correction and retraining or, in other words of *patient re education* Often re education proves most helpful and gives lasting results

Another useful technique is the diverting of the tension into useful channels Frequently the patient is relieved if his activities can be guided into channels interesting enough to cause him to devote his actions and thinking to matters where there is no immediate personal emotional strain while at the same time he secures a sense of accomplishment Many patients with gas, indigestion or headache suddenly become entirely unaware of their symptoms when they become interested in helping some less fortunate neighbor They may get release

mended for psychoneuroses are also applicable to the treatment of psychoses Certain principles of treatment are useful in the management of all psychoses while other techniques vary in their usefulness depending on the mental abnormality presented

General Measures Applicable to All Psychoses Frequently these patients are in conflict with their environment and are experiencing severe mental and often physical strain Therefore, institutional treatment is usually necessary to start proper corrective therapy Many of them are malnourished and have vitamin deficiencies and occasionally chronic infections, all of which should be corrected as promptly as possible

A program of balanced recreation and occupational therapy supervised by properly trained assistants is exceedingly useful in rehabilitation This therapy must be carefully controlled by the psychiatrist, since it is necessary to grade it according to the needs and especially the ability of the patient participating The maximum benefit is secured when this therapy is carried out in classes since the group contributes much to the development of the individual As improvement occurs, more active measures are taken until the program merges into a pattern similar to what will be required normally

Specific Therapeutic Techniques The indications for and usefulness of these measures vary depending on the mental problem presented and the patient s reaction to the treatment It is therefore necessary to consider their role in therapy under the individual psychoses

Manic depressive Psychoses

Patients exhibiting mild degrees of excitement or depression receive considerable relief from the measures outlined for the treatment of psychoneuroses In the early phase the skilled physician can do much through the proper use of psychotherapy

Hydrotherapy is useful The relaxation secured by a warm tub bath or a cold shower does much to relieve tension and reduce unpleasant excitement Simple hydrotherapy can be carried out in the patient s home Prolonged hydrotherapy requires skillful attendance and should be carried out only in institutions properly staffed and equipped to render it

In the mildly depressed patient some temporary relief may be obtained by the careful use of amphetamine (Benzedrine) sulfate 5 to 15

Azacyclonol (Frenquel) should be given in a dose of 20 mg 3 times a day and this maintained as needed This agent seems to be most beneficial in hallucinations associated with schizophrenia Meprobamate (Miltown, Equanil) may be started with 1 or 2 of the 400 mg tablets daily and increased, if necessary, to 6 of the 400 mg tablets a day without serious side effects It is occasionally helpful, especially if there is muscle tension and spasm, but usually it is not as potent as the previous drugs in releasing mental tension If depression or excessive fatigue are prominent factors, occasionally amphetamine (Dexedrine) sulfate 5 mg 2 to 4 times a day is helpful Also pipradrol (Meratran) hydrochloride 1 0 mg 3 or 4 times a day is useful Neither of these drugs influences the basic difficulty, but they are temporarily helpful until other therapy improves the patient's status As already emphasized, each of these should be used as a temporary expedient and as aids to proper psychiatric care

Many of these patients develop various muscle tensions, often followed by spasm, as a result of their mental states These produce fatigue and frequently pain, which further enhance the symptoms thus adding to the patient's difficulties Release of muscle tension or spasm can prove helpful in giving the patient considerable relief Mephenesin (Tolserol), 0 5 gm 3 to 6 times daily, is useful for this purpose Meprobamate (Equanil) 0 4-0 6 gm 4 times a day or zoxazolamine (Flexin) 1 0 to 6 0 gms daily are useful and in some patients give considerable relief Zoxazolamine given in the usual daily dose of 2 0 gm in conjunction with chlorpromazine 10 to 25 mg 3 times a day gives even better relaxation Relaxing baths, massage, heat, and various physiotherapy measures all contribute to the patient's comfort and serve to release not only muscle strain but also mental tension

Special Technical Procedures Various forms of shock therapy, narco-analysis, hypnosis, free association, dream analysis, and other specialized techniques are useful tools but must be employed only by those who have had special training Their unwise use can produce serious harm

Psychoses

Treatment of psychoses requires special psychiatric skill and training Consequently their management must be directed by a psychiatrist, and usually institutional care is necessary Many of the measures recom

tonic types of psychoses is most difficult to manage Treatment consists of physical rehabilitation, psychotherapy, drugs, and, when these measures fail, shock therapy with or without drug therapy In the extreme case which does not respond to any other measures, as a final desperate measure prefrontal lobotomy can be tried

Since approximately 25 per cent of the patients developing this disease manifest a spontaneous remission it is difficult to evaluate therapeutic measures *Certainly excellent results are occuring with drug therapy* Chlorpromazine (Thorazine) 50 to 100 mg 3 or 4 times daily is most helpful in reverting many of these patients Occasionally doses of 1 to 2 gm a day are needed for best results Usually however, the small doses *of 0 2 to 0 5 gm a day are satisfactory* The patient must be kept on the drug for long periods of time, months or even years in some cases Any patient on this drug must be observed carefully at frequent intervals for toxic effects such as jaundice anemia agranulocytosis, skin rash and hypotension *Jaundice is less common with the parenteral route*

Recent studies are suggesting that continued use of Chlorpromazine prophylactically prevents relapse in some cases of schizophrenia

Generally these patients should be hospitalized and chronic infections poor nutrition, and other remedial defects hould be corrected Occupational therapy is helpful In the paranoic type sedation and hydrotherapy, as recommended for manic depressive psychosis are also useful Unfortunately the management of the paranoic patient is fraught with danger since their delusions may lead to actions dangerous not only to themselves but also to others The possibility of homicide or suicide must be borne in mind in the mild paranoic cases petty accusations litigations and suspicions make them most difficult to handle

Psychotherapy is of value in this group of patients, but care must be taken or it may prove harmful Psychotherapy is most difficult in the paranoid schizophrenic and should be done by one highly skilled in handling this type of patent Not infrequently treatment results in serious outbursts of delusions that may suddenly change the affection the patient has toward his physician to feelings of intense hatred If there is a reasonable amount of insight there is a possibility that skilful explanation and persuasion may give relief Many of the milder cases respond readily to this treatment

Insulin shock therapy is recommended but electric shock is satisfactory if the former is not available Some believe that electric shock therapy is as effective as insulin shock therapy in those with catatonic

mg by mouth daily, d-amphetamine (Dexedrine) sulfate 5 to 15 mg daily, or pipradrol (Meratran) 1 to 2 mg 3 or 4 times a day Mild excitement on the other hand is relieved frequently by chlorpromazine (Thorazine) 10 to 25 mg 4 to 6 times a day, reserpine (Serpasil) 0 25 0 5 mg 4 times a day, or the less toxic and less effective meprobamate (Equanil) 0 4 to 0 6 gm 3 or 4 times a day Sedative drugs such as phenobarbital 15 to 30 mg 4 times a day, glutethimide (Doriden) 1 5 to 250 mg 3 or 4 times a day, or methyprylon (Noludar) 50 mg 3 or 4 times a day are all useful in mild degrees of agitation, restlessness, and excitement When insomnia is a factor the above sedatives are also useful but the hypnotic dose should be given A newer, quick acting, rapidly destroyed sedative, ethinamate (Valmid), 0 5 to 1 0 gm at bedtime is a very satisfactory agent for the quick inducement of sleep There are no after effects from it since destruction is prompt Chloral hydrate 0 5 gm by mouth 2 or 3 times a day or a dose of 1 0 gm at bedtime is an old favorite Its tendency to irritate mucous membranes sometimes precludes its use A new derivative of chloral hydrate, pentaerythritol chloral (Periclor) is devoid of the bad taste and mucous membrane irritating properties It is given in a dose of 0 3 gm 3 or 4 times daily or 0 6 to 1 0 gm at bedtime

Patients not responding to the above medical therapy and those in profound depression should be given shock therapy The most satisfactory results are obtained with electro shock therapy and from 6 to 12 treatments should be given Depressed patients should receive 2 or 3 treatments a week, but manic patients do better if 1 or preferably 2 shocks are given the first 2 days and then a treatment every other day Properly applied electro-shock therapy gives excellent results The attacks are cut short, and definite improvement or complete relief occurs in approximately 75 per cent of the patients Unfortunately this treatment does not prevent recurrence Between attacks, psychoanalyses, drug therapy, and psychotherapy should be pursued diligently If electro-shock therapy has been given an adequate trial, at least 2 courses of 15 shocks each without the patient's showing any improvement, and if the illness has been present for many years, prefrontal lobotomy should be considered as a last resort

Schizophrenias

This group, consisting of the simple paranoic, hebephrenic, and cata

satisfactory when a strong hypnotic effect is desired These drugs are also frequently helpful when given in sedative doses, sodium amobarbital (Amytal), 15 mg 4 times a day, or chloral hydrate, 0 5 gm 4 times a day, usually at mealtimes and at bedtime See also page 877

Severe cases not responding to the preceding measures should be given shock therapy in the dosage and manner recommended for manic-depressive psychosis

Patients who do not respond to these measures may be much improved by bilateral frontal lobotomy, which should be performed only as a last resort

Arteriosclerotic and Senile Psychoses

Adequate physical and mental rest simplification of the environmental demands, and activities limited to those commensurate with the patient's abilities are essential in the management of these cases

The treatment described for Arteriosclerosis is recommended for these patients A nutritious diet high in vitamins of the B complex, should be given Chronic infections should be cleared up whenever possible and overstrenuous activities reduced so that mental and physical efforts do not cause any serious drain on the patient s strength

Care must be employed in the use of hypnotic drugs in these patients since the drugs often cause confusion and further complicate management Many of these patients have insomnia which appears in the early morning hours and causes considerable distress. When indicated sodium barbital 0 3 gm by mouth at bedtime will usually prove satisfactory in relieving early morning wakefulness Sometimes acetylsalicylic acid 0 3 to 0 6 gm at bedtime is more effective than the barbiturates in producing sleep

The lives of these patients should be regulated so that useful light activities are carried on and pleasing stimulating interests are maintained

When confusion or delusion becomes severe or the patient is no longer able to cope properly with his environment institutional care is necessary

Psychotherapy and occupational therapy are useful In a few properly selected cases electro shock therapy is helpful However care must be exercised in prescribing shock treatment for these patients, since shock therapy is dangerous in patients with vascular degenerative disease

mg by mouth daily, d-amphetamine (Dexedrine) sulfate 5 to 15 mg daily, or pipradrol (Meratran) 1 to 2 mg 3 or 4 times a day Mild excitement on the other hand is relieved frequently by chlorpromazine (Thorazine) 10 to 25 mg 4 to 6 times a day, reserpine (Serpasil) 0 25 0 5 mg 4 times a day, or the less toxic and less effective meprobamate (Equanil) 0 4 to 0 6 gm 3 or 4 times a day Sedative drugs such as phenobarbital 15 to 30 mg 4 times a day, glutethimide (Doriden) 125 to 250 mg 3 or 4 times a day, or methyprylon (Noludar) 50 mg 3 or 4 times a day are all useful in mild degrees of agitation, restlessness, and excitement When insomnia is a factor the above sedatives are also useful but the hypnotic dose should be given A newer, quick acting, rapidly destroyed sedative, ethinamate (Valmid), 0 5 to 1 0 gm at bedtime is a very satisfactory agent for the quick inducement of sleep There are no after effects from it since destruction is prompt Chloral hydrate 0 5 gm by mouth 2 or 3 times a day or a dose of 1 0 gm at bedtime is an old favorite Its tendency to irritate mucous membranes sometimes precludes its use A new derivative of chloral hydrate, pentaerythritol chloral (Periclor) is devoid of the bad taste and mucous membrane irritating properties It is given in a dose of 0 3 gm 3 or 4 times daily or 0 6 to 1 0 gm at bedtime

Patients not responding to the above medical therapy and those in profound depression should be given shock therapy The most satisfactory results are obtained with electro-shock therapy and from 6 to 12 treatments should be given Depressed patients should receive 2 or 3 treatments a week, but manic patients do better if 1 or preferably 2 shocks are given the first 2 days and then a treatment every other day Properly applied electro-shock therapy gives excellent results The attacks are cut short, and definite improvement or complete relief occurs in approximately 75 per cent of the patients Unfortunately this treatment does not prevent recurrence Between attacks, psychoanalyses, drug therapy, and psychotherapy should be pursued diligently If electro shock therapy has been given an adequate trial, at least 2 courses of 15 shocks each without the patient's showing any improvement, and if the illness has been present for many years, prefrontal lobotomy should be considered as a last resort

Schizophrenias

This group, consisting of the simple paranoic, hebephrenic, and cata

stupor, excitement, panic, and confusional states Insulin shock therapy is preferable for the chronic schizophrenic patient and those with the paranoid or hebephrenic types

Patients undergoing deterioration in spite of adequate shock therapy, and who have had the disease for long periods of time, are benefited by prefrontal lobotomy This measure should be used only as a last resort, however, and with the reservation that the patient may be made considerably worse if it fails

Paranoia and Paranoid Conditions

Treatment for psychoses of this category is unsatisfactory The measures recommended for paranoid schizophrenia should be carried out These patients may become dangerous and commit serious antisocial acts They must be protected from harming both themselves and others

Involutional Psychoses

Minor degrees of this mental disturbance respond to psychotherapy and the general measures recommended for psychoneurosis Many of these patients are debilitated, have severe emotional tension, cannot sleep, eat, or relax, and have suicidal thoughts These patients should receive institutional care and be rehabilitated A nutritious diet suited to the patient's tastes, quiet, pleasant, relaxing surroundings, careful nursing attention, and relief from all strain should initiate therapy Rest, usually in bed at first, followed by a graded course of rehabilitation, occupational therapy, and gradual return to responsibilities is essential Patients must not be subjected to vigorous urging in attempts to interest them in activities

Infections, glandular hormone imbalance, and diet deficiencies should be corrected promptly Sex-hormone therapy should be given a trial since it may help considerably in relieving tension The dosage and methods of administration as previously recommended for the relief of the female and male climacteric are advised

Lack of sleep frequently constitutes a serious problem Sedation may be tried and is effective in some cases Sodium amobarbital (Amytal), 0 1 to 0 2 gm at bedtime, or chloral hydrate, 1 to 2 gm at bedtime, is

The respiration is usually in a crucial phase if paralysis involves the intercostal muscles and immediate support and splinting of the thoracic cage is imperative if the maximum value is to be gained from diaphragmatic respiration Splinting may be accomplished by a canvas belt buckled tightly around the chest just below the nipples while the chest wall is contracted A suitable band can be made by pasting 2 strips of 4 inch adhesive tape together adhesive to adhesive side and pinning this band around the contracted chest Oxygen should be given as required to prevent cyanosis The cellophane tent is the preferred method of ad ministering oxygen as the mask is generally unsatisfactory in these patients

No food or fluid should be given by mouth if abdominal distension appears or is already present the Miller Abbott tube or Wangensteen suction apparatus should be employed to relieve distension Care must be taken to prevent respiratory embarrassment from abdominal distention and treatment with the Miller Abbot tube or Wangensteen apparatus must be continued until normal peristalsis is established and the acute situation has been stabilized Hot turpentine stupes to the abdomen and a rectal tube are helpful and peristaltic action leading to expulsion of gas is frequently aided by neostigmine (Prostigmine) methyl sulfate 1 2000 given intramuscularly in 2 0 cc doses every 4 hours The bowels should be kept open by enemas until normal bowel activity returns

Bladder distention adds to abdominal distress and respiratory embarrassment and is a serious source of infection unless promptly controlled It should be prevented or relieved by inserting an inlying catheter size 12 to 16 F through the urethra the catheter may be attached to a tidal drainage apparatus or left open to promote constant drainage and maintain an empty bladder Fluids should be pushed to maintain a high urinary output During the critical phase physiological salt solution or 10 per cent dextrose solution should be given parenterally A daily urinary output of 1500 to 2000 cc is recommended Usually an intake of 4500 cc suffices

As soon as possible food should be given by mouth but during the critical phase intravenous feeding of glucose and when indicated 5 per cent amino acid hydrolysate is recommended When food can be taken orally a diet rich in vitamins and minerals containing 3000 to 3500 calories a day with from 1 5 to - gm of protein per kilogram of body weight is advised

Complete spinal shock produces total flaccid paralysis below the level of the lesion Concomitant with this is a fall in total protein in the blood

Toxic Psychoses

Psychoses in this category are caused by toxic agents and they usually respond well once the causative toxin is removed Drugs, such as the barbiturates, are common offenders Since toxic effects are more likely to occur in older patients receiving the barbiturates, they should be used with caution in older persons

Alcohol is also a frequent offender and must be withheld if abnormal psychotic effects from its use are present Patients exhibiting an alcoholic psychosis should receive large amounts, 10 to 20 times the usual daily requirement, of the B complex vitamins, a highly nutritious diet, and the measures recommended for alcoholism

BIBLIOGRAPHY

Functional Diseases of the Nervous System

1 CHENEY, C O 'Dementia Precox (Schizophrenia Group)," *Oxford Medicine*, vii Oxford University Press, p 357
2 MOSS, R E The Neuroses Their Diagnosis and Treatment, *Med Clinic No Amer*, September 1950, p 1487
3 RENNIE T A C 'Anxiety States Their Recognition and Management, *Med Clinic No Amer*, May 1948, p 597
4 ROSS, T A 'Psychoneuroses ' *Oxford Medicine*, vii Oxford University Press, p 567
5 STRECKER E A, and PEARSON, M M Psychiatric Diagnosis," *Med Clinic No Amer*, November 1951, p 1781
6 WINKELMAN N W Jr 'Chlorpromazine in the Treatment of Neuropsychiatric Disorders ' *Jour Amer Med Assoc*, 1954 CLV, 18
7 BORRUS J C Study of Effect of Miltown (2 methyl 2N Propyl 1, 3 Propanediol Dicarbamate) on Psychiatric States" *Jour Amer Med Assoc*, 1955, CLVII, 1596
8 FRIEND D G and WELLS, J C 'The Clinical Uses of Chlorpromazine *Am Pract and Digest* Treat, 1955 VI, 698

If the paralysis is of the spastic type physiotherapy should be withheld Residual spasms in muscles or muscle groups should be treated surgically as conditions indicate

As the patient s improvement warrants he should increase his activities gradually use a wheel chair increase his exercises and develop special muscle groups where they are needed The use of crutches and braces and limited ambulation should follow and gradually normal activities should be resumed

Every effort should be made to help the patient adjust to his circumstances Skillful psychotherapy is most valuable in helping him to adjust and to develop self confidence and the will to fight in a long tedious convalescence Care must be taken to see that dependence on others is kept to the minimum Occupational therapy is beneficial and social responsibilities and contacts are most desirable

Patients with penetrating spinal cord injuries usually require immediate surgery The primary indications for surgery in acute spinal cord injuries are incomplete lesions and penetrating wounds—such as those caused by a knife gunshot wound or displaced fracture fragments—that are progressing rapidly to a complete paralysis. Following surgery the procedures outlined in the preceding paragraphs are to be instituted

Acute Myelitis

The causative factor underlying this condition should be sought for and whenever possible specific therapy given In severe cases with rapidly developing paralysis the immediate measures recommended for the treatment of trauma and hemorrhage into the spinal cord are recommended Absolute bed rest is essential but great care must be taken to avoid bed sores genito urinary tract infection and other complications The measures advised in the preceding pages for trauma and hemorrhage into the spinal cord apply equally well in acute myelitis and should be instituted promptly and continued in a similar pattern for patients recovering and convalescing from the acute disease

Vigorous antibiotic therapy with penicillin streptomycin aureomycin chloramphenicol or terramycin should be given a trial the antibiotic being selected on the basis of the susceptibility of the infecting organism

Acute Epidural Abscess

This is a metastatic lesion secondary to a focal infection in the body usually a furuncle or carbuncle The onset is sudden with acute local

CHAPTER LXXV

DISEASES OF THE SPINAL CORD

The spinal cord may be impaired by various conditions, the most important of which are diseases involving trauma and hemorrhage into the spinal cord or its membranes, myelitis, acute ascending (Landry's) paralysis, degenerative myelitis or postero-lateral sclerosis, syringomyelia, and tumors

TRAUMA AND HEMORRHAGE

Hemorrhage into the spinal cord is most frequently caused by trauma, such as acute flexion of the neck and other severe injuries, but it may also result from a variety of diseases

The treatment of trauma to the spinal cord is initially concerned with the therapy of spinal shock In general, the higher the level of the lesion along the spinal axis, the more serious the condition and the poorer the outcome Spinal shock is the extent of paralysis of the motor sensory and sympathetic systems, which in the higher lesions affects the abdominal and thoracic organs, thereby increasing the complexity of treatment Lesions of the higher cervical spine are usually fatal in spite of treatment Treatment should consist of immediate bed rest and prompt measures to control shock and prevent respiratory failure with anoxemia, anoxia, and death Teamwork of surgeon, internist, and urologist is essential, if the best results are to be secured If hemorrhage has produced the lesion, it should be controlled immediately whenever possible

All patients with non-penetrating injuries of the spinal cord should be placed in a position of extension, since flexion attitudes tend to increase the lesion The patient should be placed supine with a pillow beneath the shoulders and thoracic spine Any movement of the patient from side to side should be like a log, to avoid torsion The average Gatch bed can be well adjusted to place the patient in hyperextension A hyperextension frame is advisable if available In cervical lesions it is desirable to place a sand bag on each side of the head to maintain stability

Persistent effort should be made to overcome difficulty in walking by means of re education exercises These patients should be encouraged and reassured continually about their condition Every possible effort should be made to re establish a normal type of existence Psycho therapy is helpful

In some patients with postero lateral sclerosis the presence of pernicious anemia cannot be established This is particularly true in the older age group where there is cord ischemia resulting from vascular degenerative disease Some of these patients will be helped by the administration of concentrated liver extract and vitamin B_{12} as they are used in the treatment of pernicious anemia a thorough trial of such *therapy should be given This may be supplemented by the use of potassium iodide 15 to 20 minims by mouth 3 times a day In some instances in which the spastic state predominates* mephenesin (Tolserol) 0 5 gm 3 to 6 times a day may be helpful

Acute Ascending (Landry s) Paralysis

Treatment for this acute serious paralysis should follow the pattern outlined for trauma of the spinal cord In addition the respirator should be used if respiratory embarrassment appears from the bulbar involve ment

Antibiotic therapy with aureomycin chloramphenicol or terramycin *should be given a trial*

Repeated daily lumbar punctures should be made during the acute *phase In cases that are not immediately fatal convalescence is usually* uneventful and recovery complete

Syringomyelia Gliomatosis Glioma

Treatment of this condition is unsatisfactory and in spite of therapy the disease usually progresses *Deep x ray therapy to the cord 400* roentgens a week—dorsal and ventral alternately—is helpful in relieving *vasomotor disturbances and pain The area treated with x rays should* be greater than that indicated by clinical findings Occasionally improve*ment may follow this treatment*

Myelotomy with evacuation of the syrinx fluid serves to relieve symp toms produced by compression It should be followed by x ray therapy if best results are to be secured

As a consequence of these factors, decubitus ulcers develop readily at points of pressure. The early administration of plasma proteins of concentrated serum albumin, or of a high protein diet will not effectively raise the blood protein, but after the spinal shock is past, in about 3 weeks their administration is more useful than it is earlier in combating decubitus ulcers. In the meantime all efforts must be directed toward relieving pressure by well-placed doughnut cushions beneath the sacrum, ischii, heels, trochanters and scapulae. Weight on these points should be shifted every 1½ to 2 hours and the skin gently massaged. The bed must be soft, free of wrinkles, and the bed clothing kept dry. A foam rubber mattress is helpful. Skilful, attentive nursing is essential, including keeping skin surfaces clean and dry, if bed sores are to be avoided. If an area of hyperemia develops at a pressure point, it should be cleaned well with alcohol and then painted twice daily with a mixture of equal parts of castor oil and collodion. It has been shown that if the total protein in the blood can be returned to a normal level (over 6.5 gm. per 100 cc.), the decubitus ulcer will heal more readily.

If the patient survives the acute lesion, infections tend to arise in the lungs and urinary tract. During the acute phase penicillin, streptomycin, terramycin, or aureomycin as indicated, given in the usual dosage, are helpful in combatting such infections. Penicillin 300,000 units twice a day, or streptomycin 0.5 to 1.0 gm. daily, should be given intramuscularly. Later when oral therapy is possible aureomycin or terramycin, 1.0 to 2.0 gm. by mouth daily, sulfisoxazol (Gantrisin), 1.0 to 2.0 gm. orally each day, and still later methenamine mandelate (Mandelamine), 1.0 gm. by mouth 4 times a day, are helpful in preventing genito-urinary tract infections. Tidal drainage should be continued until normal bladder function returns.

Phlebitis may develop, which in the anesthetic legs may cause little or no symptoms and yet may give rise to fatal pulmonary embolism. This complication should be watched for carefully and treated adequately.

Immediately after recovery from spinal shock and in the absence of inflammatory processes in the paralyzed parts, patients exhibiting a flaccid paralysis should have physiotherapy, gentle massage, and passive exercise several times daily to maintain supple joints and muscle tone. Simple muscle setting exercises increased as development permits are also helpful in maintaining muscle tone and preventing atrophy. Active exercises should be increased as rapidly as the patient's condition permits.

Persistent effort should be made to overcome difficulty in walking by means of re education exercises These patients should be encouraged and reassured continually about their condition Every possible effort should be made to re establish a normal type of existence Psychotherapy is helpful

In some patients with postero lateral sclerosis the presence of pernicious anemia cannot be established This is particularly true in the older age group where there is cord ischemia resulting from vascular degenerative disease Some of these patients will be helped by the administration of concentrated liver extract and vitamin B_{12} as they are used in the treatment of pernicious anemia, a thorough trial of such therapy should be given This may be supplemented by the use of potassium iodide 15 to 0 minims by mouth 3 times a day In some instances in which the spastic state predominates mephenesin (Tolserol) 0 5 gm, 3 to 6 times a day may be helpful

Acute Ascending (Landry's) Paralysis

Treatment for this acute serious paralysis should follow the pattern outlined for trauma of the spinal cord In addition the respirator should be used if respiratory embarrassment appears from the bulbar involvement

Antibiotic therapy with aureomycin chloramphenicol or terramycin should be given a trial

Repeated daily lumbar punctures should be made during the acute phase In cases that are not immediately fatal convalescence is usually uneventful and recovery complete

Syringomyelia Gliomatosis Glioma

Treatment of this condition is unsatisfactory and in spite of therapy the disease usually progresses Deep x ray therapy to the cord 400 roentgens a week—dorsal and ventral alternately—is helpful in relieving vasomotor disturbances and pain The area treated with x rays should be greater than that indicated by clinical findings Occasionally improvement may follow this treatment

Myelotomy with evacuation of the syrinx fluid serves to relieve symptoms produced by compression It should be followed by x ray therapy, if best results are to be secured

ized pain in the spine and a rapidly progressing paralysis below the level of the lesion Treatment consists of immediate surgery with drainage as soon as the diagnosis is made When the abscess can be sharply localized and lies posteriorly drainage may be accomplished by introduction into the abscess of a lumbar puncture needle, provided that the greatest care is exercised not to penetrate the meninges since purulent meningitis may result Appropriate antibiotic therapy as indicated in the previous paragraph should be started immediately and pushed vigorously

Poliomyelitis

The treatment for acute anterior poliomyelitis is described in Chapter XIII

Degenerative Lesions of the Spinal Cord Degenerative Myelitis Postero lateral Column Sclerosis

Treatment for this disease of the spinal cord should consist of measures to regulate adequately the pernicious anemia, which is usually the cause in addition to supportive measures to control pain and prevent bed sores and genito urinary tract infections, and re education exercises to overcome difficulties in walking Patients with degenerative myelitis due to pernicious anemia should receive vigorous pernicious anemia therapy as described for that disease with spinal involvement

The measures previously recommended for the prevention of bed sores and genito urinary tract infection from trauma of the spinal cord are applicable to these patients and should be carried out

A diet rich in protein, minerals, and vitamins is recommended Supplementary vitamin therapy with vitamins of the B complex, especially B_1 is advised Folic acid should not be given Dilute hydrochloric acid as recommended for pernicious anemia, may be helpful

If not severe, pain may be controlled with acetylsalicylic acid 0 3 to 0 6 gm by mouth 2 or 3 times a day Severe pain may require codeine phosphate, 30 to 60 mg by mouth 1 or 2 times a day, or meperidine (Demerol) hydrochloride 50 to 100 mg by mouth 1 or 2 times daily

If there is an associated infection antibiotic therapy selected in relation to the susceptibility of the infecting organism should be carried out Restlessness may be relieved by the administration of phenobarbital, 0 1 gm at bedtime unless it decreases co-ordination, if so chloral hydrate should be used

CHAPTER LXXVI

DISEASES OF THE BRAIN AND MENINGES

In this section will be considered those conditions whose manifestations are chiefly or entirely localized in the brain and are due to disturbance of brain substance sometimes from infections often from trauma or from lesions of the blood vessels

Aphasia Apraxia Agnosia

The treatment of such disturbances as aphasia apraxia and agnosia is based on the concept that their function is localized in a dominant (major) hemisphere of the brain When this hemisphere (Brodmann areas 37 21 and 22) becomes altered by disease the minor (latent) hemisphere is called upon to take over the lost function In an attempt to train the function of the minor hemisphere endurance rather than capacity is developed and the efficiency of the former major area is never attained except in early childhood This is the reason that attempts at restoration of such lost functions in adult life are so much more difficult than in childhood

The institution of treatment in aphasia apraxia or agnosia depends first on a proper recognition of the defect that exists When properly established the individual must be re-educated in the desired functions as one would teach an infant and a child The engrams to be trained are in existence in the minor hemisphere but they are crude and have gone without use during most of the patient s life The aim is therefore, to develop these in place of the lost functions of the major hemisphere Such re education requires the greatest care and patience Objects are named repeatedly and distinctly while the object in question is exhibited Exaggerated movements may be necessary as in pantomime The teacher s speech must be slow clear and painstakingly distinct One should begin with detached letters and advance slowly to words with one syllable Reading and writing are taught as one would teach a child If the right hand is paralyzed the left hand is to be trained

Tumors of the Spinal Cord

A tumor of the spinal cord must always be considered in every patient presenting any long tract signs Only by such an awareness, with proper diagnosis, can correct treatment be carried out The treatment for spinal cord tumor is proper surgical excision, unless it can be demonstrated to be metastatic Whether primary or metastatic tumor is found, after proper verification of the pathological histology, deep roentgen therapy may be desirable In the case of gumma of the spinal cord, treatment should be given as outlined under Syphilis

A word of caution should be given concerning diagnostic lumbar puncture in any case suspected of having a tumor of the spinal cord If a myelitis or any paralysis results following the spinal tap surgical decompression by laminectomy must be carried out *immediately* or irreparable damage may follow quickly

BIBLIOGRAPHY

Diseases of the Spinal Cord

1 HADDEN S B 'Diagnosis of Spinal Cord Disease, *Med Clinic No Amer*, November 1951 p 1765
2 HEUSNER A P Nontuberculous Spinal Epidural Infections *N E J Med*, 1948 ccxxxix, p 845
3 MUNRO D The Care of Patients Paralyzed as the Result of Injury to the Spinal Cord and Cauda Equina, *Med Clinic No Amer*, September 1949 p 1273

times a day is helpful Occasionally a hypersensitive carotid sinus must be denervated in order to prevent attacks In stagnant anoxia as in active or passive congestion of the brain (hyperemia) from cardiac failure local trauma to the brain and polycythemia vera the treatment should consist of an attempt to improve the circulation of the brain and the restoration of proper oxygen consumption The therapy for cardiac failure should be carried out when it is present In closed head injury with primary shock and relative hemoconcentration, the use of plasma intravenously and oxygen inhalation are recommended In histotoxic anoxia cerebral oxygen consumption is deficient because of the presence of metabolites in the circulating blood as seen in uremia If the renal insufficiency is acute and temporary as with extra renal azotemia treatment for that condition should be carried out The toxic metabolites also may be removed successfully by the use of the artificial kidney

Cerebral Edema

Cerebral edema is a condition of swelling of brain substance either localized or generalized from intra and extra cellular fluid retention associated with local pathological changes such as tumor or trauma or as a manifestation of systemic disorder as in cardiac failure uremia sepsis and cachectic states

Cerebral edema is a reversible process if it is not too extensive and severe The maintenance of cerebral circulation with adequate oxygen is most important since the preservation of brain cells depends primarily on two factors (1) adequate oxygen and (2) glucose

In instances where the edema is not associated with tumor or abscess internal decompression by medical means should be used This should include (1) lumbar puncture (2) hypertonic solutions given intravenously and (3) withholding of fluids The last two are dehydrating methods In obese individuals whose general state of hydration is thought to be greater than in thin individuals more vigorous dehydration than this may be necessary to be effective in the treatment of cerebral edema

A lumbar puncture should not be performed in the presence of an intracranial space occupying lesion since its effect is of very short duration and it may do the patient great harm by altering the intracranial dynamics through displacement of brain tissue In generalized edema from other causes the procedure is relatively safe if done in the following manner The patient should be placed lying on his side never

Often patients with one or more of these disturbances are very emotional irritable, and easily discouraged, requiring the utmost diligence in their management Usually drugs have no place in the treatment of these respective disturbances, although mild sedatives may be used, such as phenobarbital 15 mg 2 or 3 times a day, for nervous irritability Constant encouragement is necessary

Affections of the Blood Vessels

In affections of the blood vessels of the brain, arteries are chiefly concerned in the production of symptoms These consist primarily of narrowing of the vessels without or with thickening of their walls, obstruction of the lumen of the vessels, and hemorrhage Significant venous involvement consists primarily in passive congestion or infection

Cerebral Anemia and Anoxia

Severe acute hemorrhage with loss of blood from the body can produce a cerebral anemia with variable neurological manifestations from syncope to transient paralyses and even blindness in severe cases The treatment should consist of keeping the patient quiet and warm with the head lower than the body, giving caffeine, whiskey, oxygen and immediate transfusion of whole blood to replace circulating blood volume

Cerebral anoxia can be classified as anemic anoxia, anoxic anoxia, stagnant anoxia and histotoxic anoxia In anemic noxia there is insufficient blood to carry the oxygen to the brain In anoxic anoxia, as seen in carbon monoxide poisoning and nitrous oxide anesthesia, there is insufficient oxygen available in the circulating blood The treatment for both of these types is the adequate administration of oxygen preferably by the nasopharyngeal catheter method, and increasing the oxygen carrying mechanism by transfusions of fresh whole blood or relief of the circulatory impairment when possible To stimulate respiration caffeine sodium benzoate should be given as long as needed in doses of 0 5 gm intravenously every hour 5 per cent carbon dioxide with 95 per cent oxygen may also be helpful when inhaled for 3 to 5 minutes until the patient is hyperventilating this may be repeated as often as every 20 to 30 minutes Care must be taken, however, that the carbon dioxide does not further embarrass an already depressed respiration If a hypersensitive carotid sinus is causing sudden fall in blood pressure and severe circulatory impairment, the use of ephedrine sulfate 25 to 50 mg 3 times a day, and tincture of belladonna, 15 to 20 drops 3 or 4

may be used as by the administration of sodium phosphate, 4 to 8 gm every morning on arising or every other morning as indicated For prolonged use sodium phosphate is less drastic than magnesium sulfate and consequently preferable

Cerebral Hemorrhage Embolism and Thrombosis

In these various cerebrovascular accidents it is of great importance that a correct diagnosis of the pathological lesion be made if possible in order that the best treatment be carried out prognosis for recovery is somewhat better in cases of embolism or thrombosis than of hemorrhage thereby making treatment appear more effective Furthermore anticoagulants recommended by some for embolism or thrombosis are contraindicated in cases of hemorrhage

Cerebral Hemorrhage

The treatment for cerebral hemorrhage depends somewhat upon the location of the bleeding If it is in the usual site in the internal capsule with resulting contralateral hemiplegia no attempt should be made to enter the skull surgically to try to stop bleeding The patient should be placed at complete bed rest in a position such that breathing is not obstructed the pharynx should be aspirated repeatedly to keep the respiratory passages clear Oxygen should be given continuously until the condition becomes stabilized Lumbar puncture should be performed carefully to reduce increased intracranial pressure and to determine the relative degree of hemorrhage However it should be emphasized that the absence of red blood cells from the spinal fluid removed by lumbar puncture does not necessarily mean that hemorrhage has not occurred in approximately 15 per cent of cases of cerebral hemorrhage the lesion is so small or so situated that the blood does not penetrate the cerebrospinal fluid space Repeated spinal punctures are usually of no value If blood is present in the spinal fluid the Queckenstedt test (jugular compression during spinal tap) should not be performed If diagnostic lumbar puncture has not been carried out or if it is contraindicated irritative phenomena from blood in the cerebrospinal fluid space as manifested by stiffness of the neck and the degree of unconsciousness are signs that there has been bleeding With intracerebral hemorrhage unconsciousness is the rule often it is not so marked with embolism and thrombosis

If the hemorrhage and surrounding edema is small and circumscribed

Often patients with one or more of these disturbances are very emotional, irritable, and easily discouraged, requiring the utmost diligence in their management Usually drugs have no place in the treatment of these respective disturbances, although mild sedatives may be used, such as phenobarbital 15 mg 2 or 3 times a day, for nervous irritability Constant encouragement is necessary

Affections of the Blood Vessels

In affections of the blood vessels of the brain, arteries are chiefly concerned in the production of symptoms These consist primarily of narrowing of the vessels without or with thickening of their walls, obstruction of the lumen of the vessels and hemorrhage Significant venous involvement consists primarily in passive congestion or infection.

Cerebral Anemia and Anoxia

Severe acute hemorrhage with loss of blood from the body can produce a cerebral anemia with variable neurological manifestations from syncope to transient paralyses and even blindness in severe cases The treatment should consist of keeping the patient quiet and warm, with the head lower than the body giving caffeine, whiskey, oxygen, and immediate transfusion of whole blood to replace circulating blood volume

Cerebral anoxia can be classified as anemic anoxia, anoxic anoxia, stagnant anoxia, and histotoxic anoxia In anemic noxia there is insufficient blood to carry the oxygen to the brain In anoxic anoxia as seen in carbon monoxide poisoning and nitrous oxide anesthesia there is insufficient oxygen available in the circulating blood The treatment for both of these types is the adequate administration of oxygen, preferably by the nasopharyngeal catheter method and increasing the oxygen carrying mechanism by transfusions of fresh whole blood or relief of the circulatory impairment when possible To stimulate respiration caffeine sodium benzoate should be given as long as needed in doses of 0 5 gm intravenously every hour, 5 per cent carbon dioxide with 95 per cent oxygen may also be helpful when inhaled for 3 to 5 minutes until the patient is hyperventilating, this may be repeated as often as every 20 to 30 minutes Care must be taken, however, that the carbon dioxide does not further embarrass an already depressed respiration If a hypersensitive carotid sinus is causing sudden fall in blood pressure and severe circulatory impairment, the use of ephedrine sulfate 25 to 50 mg 3 times a day, and tincture of belladonna 15 to 20 drops 3 or 4

may be used as by the administration of sodium phosphate 4 to 8 gm every morning on arising or every other morning as indicated For prolonged use sodium phosphate is less drastic than magnesium sulfate and consequently preferable

Cerebral Hemorrhage Embolism and Thrombosis

In these various cerebrovascular accidents it is of great importance that a correct diagnosis of the pathological lesion be made if possible in order that the best treatment be carried out prognosis for recovery is somewhat better in cases of embolism or thrombosis than of hemorrhage thereby making treatment appear more effective Furthermore anticoagulants recommended by some for embolism or thrombosis are contraindicated in cases of hemorrhage

Cerebral Hemorrhage

The treatment for cerebral hemorrhage depends somewhat upon the location of the bleeding If it is in the usual site in the internal capsule with resulting contralateral hemiplegia no attempt should be made to enter the skull surgically to try to stop bleeding The patient should be placed at complete bed rest in a position such that breathing is not obstructed the pharynx should be aspirated repeatedly to keep the respiratory passages clear Oxygen should be given continuously until the condition becomes stabilized Lumbar puncture should be performed carefully to reduce increased intracranial pressure and to determine the relative degree of hemorrhage However it should be emphasized that the absence of red blood cells from the spinal fluid removed by lumbar puncture does not necessarily mean that hemorrhage has not occurred in approximately 15 per cent of cases of cerebral hemorrhage the lesion is so small or so situated that the blood does not penetrate the cerebrospinal fluid space Repeated spinal punctures are usually of no value If blood is present in the spinal fluid the Queckenstedt test (jugular compression during spinal tap) should not be performed If diagnostic lumbar puncture has not been carried out or if it is contraindicated irritative phenomena from blood in the cerebrospinal fluid space as manifested by stiffness of the neck and the degree of unconsciousness are signs that there has been bleeding With intracerebral hemorrhage unconsciousness is the rule often it is not so marked with embolism and thrombosis

If the hemorrhage and surrounding edema is small and circumscribed

sitting up, for fear of brain stem herniation An 18 gauge needle should be used for the tap The initial spinal fluid pressure must be determined, preferably with an Ayer water manometer attached to a 2 or 3 way stop-cock The normal pressure is 100 to 200 mm of water If the initial pressure is over 200 mm of water, sufficient fluid should be removed to lower the pressure to one-half the original pressure If the original pressure is exceedingly high (500 to 600 mm water), the pressure should be brought down only to one-half, and 6 to 8 hours later the tap should be repeated, use the same technique and rule of reduction, until the pressure is finally brought below 200 mm water The quantity of fluid removed is inconsequential as long as pressure relationships are maintained as just indicated

For the method of decompression by dehydration, a venesection with removal of 400 to 500 cc of blood is helpful when it can be carried out A 25 per cent solution of dried serum albumin administered intravenously to a total dose of 60 to 80 cc in a period of 8 to 10 minutes is also effective The patient should not be permitted to take any fluid for the next 8 hours Rarely is it necessary to repeat this dose, but it can be done after this 8 hour period Hypertonic sugar solutions are also useful Glucose is preferable to sucrose, previously often recommended, because it is available gives the necessary carbohydrate for brain cell metabolism and is not injurious to the kidneys It is best used in 50 per cent concentration in doses of 50 to 100 cc for adults, 25 to 50 cc for children If the cerebral edema is associated with alcoholism, glucose is best administered as a 10 per cent solution in 1000 cc sterile distilled water since the patient needs fluid with a mild dehydrating effect on the brain Intramuscular injection of a 25 per cent magnesium sulfate solution in a dose of 0 2 to 0 4 cc per kilogram of body weight is often valuable Because the sodium ion possesses fluid retention properties normal saline solution should not be used in patients with cerebral edema unless there is a direct indication for the need of sodium chloride

A much slower method of cerebral dehydration is the withholding of fluids by mouth In order that renal excretion of waste products may be maintained the minimal fluid intake for 24 hours must be 1500 cc, provided the kidneys are normal Care must be exercised that the patient does not go into a state of toxic dehydration If the patient with cerebral edema is unconscious it is best to pass a nasal feeding tube and give nourishment and fluids by the gastro-intestinal route rather than to give it by repeated intravenous infusions

In states of mild cerebral edema a method of dehydration by catharsis

depress respiration as much Sodium amobarbital (Amytal), 0 1 to 0 4 gm and phenobarbital 0 1 to 0 3 gm daily are helpful in combatting restlessness

In younger individuals with cerebral vessel aneurism and without hypertension and arteriosclerosis *operation after bleeding stops* is being recommended more and more The best results in localization of the aneurism are to be obtained by arteriography If the ruptured aneurism seems accessible to the neurosurgeon operation with tying off of the proximal and distal vessels may be tried However, experience has shown that a second rupture is almost inevitable although it may be years before it occurs

Subdural Hematoma

In subdural hematoma proper localization with trephining and removal of the clot should be carried out It is to be remembered that such hematomata may be bilateral or localized by contra-coup Consequently *trephining over both hemispheres is advisable* After care should be directed to the management of cerebral edema and the re establishment of fluid balance as outlined under treatment for Cerebral Edema Early ambulation is advised for these patients

Extra dural Hematoma

For extra dural hematoma operation and removal of the extra dural clot is mandatory as soon as the diagnosis is made Usually if not operated upon within the first 18 hours after onset the patient will die even though the operation has been carried out successfully The after care is the same as that outlined for the treatment of Cerebral Edema

Cerebral Embolism

The general principles of treatment of cerebral embolism are the same as for any cerebral vascular accident hemorrhage embolism or thrombosis as outlined in the preceding pages under Cerebral Hemorrhage

The most common variety of cerebral embolism is from a clot located in the left heart cavity formed and set free during cardiac arrhythmia particularly auricular fibrillation or flutter especially in the presence of mitral stenosis Extrasystoles heart block or prolonged paroxysmal

consciousness will usually be regained in a few hours or in several days. During the period of unconsciousness, the patient should be given nourishment and fluid through a stomach tube. He should be turned frequently to prevent pulmonary hypostasis and pneumonia. An antibiotic should be given as a preventive measure against infection. After consciousness is regained, a liquid and soft solid diet should be instituted and passive exercise to the paralyzed extremities begun. Careful daily observation of cardiac and respiratory function should be made and if pneumonia or cardiac failure develops, it should be treated. If unconsciousness continues for more than a few hours, a catheter should be inserted into the bladder for constant drainage. A possible complicating urinary tract infection should be watched for carefully and, if found, treated thoroughly. Attention should be given to bowel function with enemas or a mild cathartic as needed, preferably the former.

Any underlying conditions as hypertension, cardiac insufficiency, diabetes mellitus, or other diseases should receive proper therapy as outlined under such headings.

When the hemorrhage is a large one, resulting in unconsciousness for many days, the condition will usually be fatal irrespective of treatment. Unless an underlying operable condition such as tumor with hemorrhage or an accessible aneurism has been found, operation in these patients should not be carried out.

Spontaneous Subarachnoid Hemorrhage. Rupture of Congenital Aneurism

In spontaneous subarachnoid hemorrhage, usually due to rupture of a congenital aneurism of a cerebral vessel, immediate operation is not advised. The treatment for the immediate attack should be the same as outlined in the paragraphs on cerebral hemorrhage. In subarachnoid hemorrhage, however, several spinal taps may be necessary, as outlined under Cerebral Edema, to reduce the intracranial pressure to normal and should be performed daily or every few days. No attempt should be made to remove all the blood by spinal puncture. If the prothrombin is depressed, vitamin K, 2 to 4 mg., should be given intramuscularly daily. The patient must be kept at absolute rest and fed by an attendant for 4 to 6 days after regaining consciousness.

For severe headache, codeine phosphate, 30 to 60 mg., or meperidine (Demerol) hydrochloride, 50 to 150 mg., should be given every 3 or 4 hours. These drugs are better than morphine sulfate since they do not

disease after the thyrotoxicosis has been treated properly and (3) with organic valvular heart disease with little or no cardiac enlargement or cardiac failure in whom the auricular fibrillation has been of relatively short duration several weeks to several months For this we recommend quinidine sulfate or quinidine preceded by digitalis as described for Cardiac Arrhythmias

With cerebral embolism from intramural thrombi following myocardial infarction the incidence of such embolism may be lessened by the prophylactic use of anticoagulant therapy In this circumstance anticoagulant therapy is advised In the event of a cerebral embolus occurring during treatment of myocardial infarction with anticoagulants the anticoagulant should be continued in treatment of the myocardial infarction and therapy for cerebral embolism using stellate ganglion block should be given as outlined in the preceding paragraphs

When cerebral embolism results from vegetations from bacterial endocarditis *anticoagulant therapy should not be used since experience* has shown that further complications are apt to develop particularly cerebral hemorrhage On the other hand intensive antibiotic therapy should be instituted with the drug most effective against the offending organism The treatment of the neurological involvement from cerebral embolism of vegetative origin should be stellate ganglion block as outlined for Cerebral Embolism If an infected embolus causes a brain abscess, it should be treated as outlined under Brain Abscess

Cerebral Fat Embolism

Usually but one of the components of a universal fat embolism cerebral fat embolism occurs most commonly after fractures of bones but may occur without injury and particularly after prolonged ether anesthesia If the fat embolism is severe the outcome is usually fatal

The treatment of cerebral fat embolism is largely symptomatic If severe enough to be recognized sodium dehydrocholate (Decholin) 200 to 300 cc of a 20 per cent solution should be given intravenously daily until recovery To enhance the effect of sodium dehydrocholate as well as to dilate the pulmonary capillaries papaverine may be tried in intravenous doses of 30 mg every hour or two This treatment may cause icterus for 24 to 48 hours Circulatory stimulants such as caffeine sodium benzoate 0 5 gm may also be given intravenously at 3 to 4 hour intervals

consciousness will usually be regained in a few hours or in several days During the period of unconsciousness, the patient should be given nourishment and fluid through a stomach tube He should be turned frequently to prevent pulmonary hypostasis and pneumonia An antibiotic should be given as a preventive measure against infection After consciousness is regained, a liquid and soft solid diet should be instituted and passive exercise to the paralyzed extremities begun Careful daily observation of cardiac and respiratory function should be made, and if pneumonia or cardiac failure develops, it should be treated If unconsciousness continues for more than a few hours, a catheter should be inserted into the bladder for constant drainage A possible complicating urinary tract infection should be watched for carefully and if found, treated thoroughly Attention should be given to bowel function with enemas or a mild cathartic as needed, preferably the former

Any underlying conditions as hypertension, cardiac insufficiency, diabetes mellitus or other diseases should receive proper therapy as outlined under such headings

When the hemorrhage is a large one, resulting in unconsciousness for many days, the condition will usually be fatal irrespective of treatment Unless an underlying operable condition such as tumor with hemorrhage or an accessible aneurism has been found, operation in these patients should not be carried out

Spontaneous Subarachnoid Hemorrhage Rupture of Congenital Aneurism

In spontaneous subarachnoid hemorrhage, usually due to rupture of a congenital aneurism of a cerebral vessel, immediate operation is not advised The treatment for the immediate attack should be the same as outlined in the paragraphs on cerebral hemorrhage In subarachnoid hemorrhage, however, several spinal taps may be necessary, as outlined under Cerebral Edema to reduce the intracranial pressure to normal and should be performed daily or every few days No attempt should be made to remove all the blood by spinal puncture If the prothrombin is depressed vitamin K, 2 to 4 mg, should be given intramuscularly daily The patient must be kept at absolute rest and fed by an attendant for 4 to 6 days after regaining consciousness

For severe headache codeine phosphate 30 to 60 mg or meperidine (Demerol) hydrochloride, 50 to 150 mg should be given every 3 or 4 hours These drugs are better than morphine sulfate since they do not

phalon, or occipital lobes of the brain Previously attributed to vaso spasm, it may result from aneurysm, vessel stenosis or partial occlusion by thrombosis When one can feel quite certain that cerebral hemorrhage with infarction is not present and that there is no other evident cause for the intermittent symptoms (tumor abscess etc) anticoagulant therapy should be tried If rapid effect is necessary, heparin should be used In the usual case bishydroxycoumarin (Dicumarol) or phenin dione (Hedulin Indon) may be used The latter is given in a dosage similar to bishydroxycoumarin and may give a more uniform prothrom bin level for long term administration The method of use of bishydroxycoumarin is discussed under coronary occlusion, page 737

Thrombosis of cerebral sinuses and veins may be primary but usually they are secondary to infection in the contiguous structures such as the ear mastoid or air sinuses of the skull The use of chemotherapy and antibiotics has greatly lessened the incidence of these forms of thrombosis Furthermore, with their occurrence the use of such agents as penicillin streptomycin and chloramphenicol singly or together in large doses has proved to be life saving but the condition remains a serious problem, and complete reliance should not be placed on anti biotics alone Proper surgical intervention including ligation and thrombus removal should be carried out if feasible

Rehabilitation following cerebral vascular diseases The attitude toward the care of physical disability following cerebral hemorrhage embolism or thrombosis has changed from a negative to a distinctly positive one No longer is it acceptable to be satisfied with saving life now every effort should be made by a graduated program to restore as much function as is possible to make the individual self sufficient and to return him to gainful occupation This requires much diligent encouragement and patience on the part of both physician and patient To avoid contractures passive motion should be started early with a full range of motion As a guide to progress, if the patient can move the affected arm he probably will be able to walk again since in hemiplegia the arm usually is affected more severely than the leg Further, if the affected leg can be flexed on to the chest it indicates sufficient quadriceps power to learn to walk again

The following outline is recommended by Rusk

The objectives of a program of rehabilitation for the hemiplegic pa tient are (1) to prevent deformities (2) to treat deformities if they occur (3) to retrain the patient in ambulation and elevation activities

tachycardia can cause intracardiac thrombi and result in embolism but do so less commonly. With all of them, associated cardiac failure predisposes to cerebral embolism. Cardiac failure, when present, should be treated thoroughly.

For the local cerebral circulatory disturbance associated with embolism, stellate ganglion block may be helpful particularly when done early. The principle consists of anesthetizing the cervical sympathetic chain on the side of the lesion to produce vasodilatation of the collateral circulation surrounding the point of obstruction. The usual injection should consist of 20 cc. of 1 per cent procaine hydrochloride introduced into the angle between the body and the transverse process of one of the lower cervical vertebrae, usually C 5 or C 6. It is not necessary to inject the ganglion directly. It is desirable to give 0.12 gm. of sodium phenobarbital intramuscularly 15 to 30 minutes before the procaine block to guard against a reaction. A successful block will be evidenced by the appearance of a Horner's syndrome and by the patient's feeling fullness in the ipsolateral naris. The return of cerebral function may be dramatic. If temporary improvement is followed by relapse, the injection should be repeated.

After an embolus to the brain or elsewhere has occurred, a decision must be made whether or not treatment should be directed toward re-establishment of normal cardiac sinus rhythm. In paroxysmal tachycardia there is no choice other than to stop the rapid heart action, for it alone can lead to death. In the other arrhythmias, however—extrasystoles, auricular fibrillation, and auricular flutter when the ventricular rate is reasonably normal, 60 to 90—the individual is in no immediate danger to life as far as the heart is concerned but is in danger from a cerebral embolus. Some feel that regardless of the duration of the arrhythmia, especially auricular fibrillation, if no contraindications to the use of anti-fibrillatory drugs exist—such as great cardiac enlargement, cardiac failure, or defective intracardiac conduction—an attempt should be made to re-establish a regular rhythm. Experience has shown that cerebral embolism occurs more often after reversion to a sinus rhythm than it does if the auricular fibrillation persists. Once an embolus has occurred in the presence of auricular fibrillation, it does not necessarily follow that more will occur, thereby requiring treatment to establish a normal sinus rhythm. It is our opinion that the attempt to establish a normal sinus rhythm should be considered in those individuals (1) who have auricular fibrillation with no underlying heart disease, (2) in whom auricular fibrillation complicates thyrotoxic heart

ankle stop, and a supinator "T" strap should be prescribed to prevent plantar flexion and supination of the foot and give the patient confidence so that he will flex his knee and hip With the brace and a cane in the unaffected hand for balance, most hemiplegic patients soon learn to walk unaided

A patient with flaccid hemiplegia will be unable to make a voluntary movement when in the supine position If, however, the patient is held in the erect position with the affected lower extremity on the floor, he will flex and extend the leg as in walking and be able to bear his body weight The sensory contact of the foot on the floor stimulates the reflex pattern of walking Ambulation should be the first procedure in a rehabilitation program since it can be accomplished by the majority of patients

Some patients especially those in the younger age groups, learn to walk with a good reciprocal pattern without the aid of a cane No patient, however, seems to learn the reciprocal arm pattern without special training

The normal pattern of walking is to move the right arm and left leg forward and then the left arm and right leg The hemiplegic patient walks with the affected arm motionless adducted, and partially flexed at the elbow It is necessary to break this pattern of walking if the patient is to have the appearance of being normal

The following methods are recommended for retraining in the normal pattern of walking

Method I Retraining in walking

Equipment Parallel bars with a sliding apparatus over the bars to prevent excoriation of the hands (Round cardboard boxes with the ends removed can be placed over the bars The open sides can be taped together with adhesive tape to hold them on the bars

Position Stand between the bars with one hand on each bar The affected hand is placed on the moveable box and may be tied if necessary

Instructions Step forward with the right foot and move the left hand forward along the bar Step forward with the left foot and move the right hand along the bar

Repeat five times several times a day up to fatigue

Method II Retraining in walking

Equipment None

Position Standing with feet together and arms at the side

Instructions Step forward with the right foot and swing the left arm

Cerebral Thrombosis

Thrombosis in cerebral vessels is much more common than is often thought Some believe that cerebral thrombosis precedes most cases of non-traumatic hemorrhage, and on that basis proper therapy of the thrombosis may prevent cerebral hemorrhage Immediate treatment should be bed rest with the head low and fluids as needed

If the cerebrovascular accident can be recognized promptly as one of thrombosis, considerable benefit may be obtained by the immediate intravenous injection of 500 mg of procaine hydrochloride dissolved in 500 cc of saline solution Even better is the injection of procaine into the cervical sympathetic ganglia on the homolateral side of the lesion (nerve block) as outlined under Cerebral Embolism Ganglion block must be done by one skilled in the technique if best results are to be obtained and serious accidents are to be avoided Nicotinic acid (Niacin) 50 mg 4 times a day by mouth, and wine or whiskey, 30 cc every 2 hours, have a dilating effect and are helpful

A clinical picture simulating cerebral thrombosis may result from chronic carotid artery occlusion, in some of these cases lowering the blood pressure markedly may prove dangerous and place the patient's life in jeopardy, and therefore the blood pressure should be maintained

Recent experience suggests the use of anticoagulant therapy in the treatment of thrombosis This is particularly desirable for thrombosis associated with polycythemia vera—more so than in arteriosclerosis, where it is primarily the vessels that are diseased If it can be fairly well established that the condition is one of thrombosis, the careful institution of bishydroxycoumarin (Dicumarol) is indicated, in the same manner as outlined for myocardial infarction Care must be taken not to depress the prothrombin concentration below 30 or 35 per cent.

If the cerebral thrombosis is on a syphilitic basis, treatment should be carried out as for benign late syphilis, with large doses of iodides 3 times a day after meals

Syndrome of Intermittent Insufficiency of the Basilar Arterial System

Recently isolated as a more specific syndrome, vascular insufficiency of the basilar arterial system is characterized by intermittent transitory symptoms of impaired function of some portion of the pons, mesence

Exercise I Flexion of the arm at shoulder

Purpose To maintain, or increase the shoulder movements and to strengthen the shoulder girdle muscles

Positions Sitting on a chair or lying supine in bed

Instructions The patient grasps the wrist of the affected arm with the fingers of the unaffected arm He raises the arms forward and upward as far overhead as possible *Repeat five times on the hour*

Exercise II Flexion and extension of the forearm

Purpose To obtain full range of motion at the elbow and active flexion and extension of elbow without adduction

Position Sitting on a chair elbows close to side of body and palms of the hands together with the ulnar side of the hands resting on the affected knee

Instructions The patient flexes the forearms and touches the chin Repeat *five times on the hour*

The patient *may have difficulty in opening the spastic fingers with the* unaffected fingers but the best possible position should be obtained This is a good exercise in preventing flexion contractures of the fingers

It is an interesting neuromuscular phenomenon that when the hands are clasped or even brought in contact the elbow can be flexed without any adduction of the shoulder When the hands are separated and the patient is asked to flex the elbow the affected arm will adduct and rotate inward

Exercise III Flexion and extension of the forearm and supination and pronation of the hand

Purpose To combine flexion and extension of the elbow with supination and pronation of the hand

Position As in Exercise II

Instructions The patient places his *palms together as in Exercise II, flexes the forearm and supinates the affected* hand as he raises it to the chin On extension of the forearm the hand is pronated

Repeat five times on the hour

The tight supinator muscles of the affected arm can be stretched by the unaffected hand Flexion of the elbow with supination of the hand are the most useful movements in performing the activities essential for daily living

(4) to teach the patient to perform the activities of daily living and working with the unaffected arm and hand, (5) to retrain the affected arm and hand to the maximum capacity, and (6) to treat facial paralysis and speech disability if present

Prevention of Deformities The spastic hemiplegic patient, when lying in bed, holds the upper extremity in adduction and internal rotation with the elbow, wrist, and fingers of the affected part in a flexed position. The affected lower extremity is usually flexed and adducted at the hip joint, the knee is flexed, and the ankle is plantar flexed and supinated

If treatment is started within a few days following the cerebral vascular accident, there is no need for any special procedures to protect the affected limbs If, however, the patient must remain in bed for a period of time, procedures must be instituted to prevent deformities

A posterior ankle splint is used to prevent shortening of the heel cord A pillow in the axilla will prevent adduction and internal rotation of the shoulder joint, a frequent residual deformity in hemiplegia. Passive movements of the arm in abduction, external rotation, and in the over head position should be performed several times a day to prevent a "frozen shoulder"

Treatment of Deformities The principal deformities which may occur are "frozen shoulder" and a shortened heel cord The use of heat and massage to the arm and shoulder is of value in preparing the part for stretching Passive movements of the shoulder are useful in increasing the range of motion These movements can be performed by a therapist, nurse, or by the patient himself (see Exercises I and II)

A short heel cord seldom requires operative procedures The heel cord usually can be lengthened by means of stretching and a short leg brace with a 90-110 degree stop at the ankle to maintain the gains made by stretching and ambulation

Ambulation Flexion and extension movements at the hip and knee usually can be performed by the spastic hemiplegic subject who is started on early ambulation When, however, the hip and knee are flexed, as in walking, the foot dorsiflexes and supinates The patient is usually afraid to place the supinated foot on the floor because of the danger of injuring the ankle or falling To prevent this foot movement he walks with a fixed knee joint and circumducts the lower extremity This slow awkward gait if used for a long time will give the patient a pattern of walking which will be cumbersome, fatiguing, and difficult to correct

A double bar, short leg brace with a stirrup attachment, 90 degree

Exercise VI Extension of fingers and thumb

Purpose As in Exercise V

Position Sitting on a chair with hand resting on table in pronation and fingers extended as far as possible

Instructions Press backward and downward on the table surface so that the palm of the hand is in contact with the table

Repeat five times on the hour

Exercise VII Extension and flexion of fingers and thumb

Purpose To produce passive movements of extensors and active movements of flexors

Position As in Exercise VI with a pencil resting on the table under the palm of the hand

Instructions Press backward and downward on the dorsal surface of the hand so that palm of hand is in contact with the table Release pressure, flex the fingers and pick up the pencil

Repeat five times on the hour

Cerebral Palsies of Children Agenesia Little's Disease

In this group are included prenatal developmental anomalies postnatal infections encephalitis et cetera as well as natal hemorrhages due to birth injury

When hemorrhage due to trauma can be established to be present, evacuation of the clot should be attempted In the majority of cases of infantile cerebral palsy however there is defective brain tissue for which neurosurgical treatment has been most disappointing Partial section of peripheral nerves to certain of the affected muscles may be of benefit, however Such procedures as posterior root section, sympathectomy and section of vestibulo spinal and reticulo spinal tracts in the spinal chord have generally been without benefit and are not advised At the same time certain orthopedic procedures such as tenotomy, muscle transplants, and deformity corrections may be of great value if done early

Because of the mental as well as neuromuscular involvement in these individuals it is wisest to adopt a general plan of therapy to cover the total personality of the individual as well as the deformities This should include emotional and personality adjustments as well as proper

forward and point to the right foot Step forward with the left foot and swing the right arm forward and point to the left foot The opposite arm and leg must be moved together and remain parallel at all times

Repeat five times several times a day

For children a red ribbon is tied to the right wrist and left foot and a yellow ribbon to the left wrist and right foot The children are instructed to move the red ribbons foward and then the yellow ribbons

When the patient can walk with the reciprocal pattern of arm and leg movements and talk with the instructor, the pattern is formed and the patient is retrained

The Unaffected Arm and Hand As a return of function in the affected upper extremity cannot usually be expected for a long period of time, if ever, it is essential to teach the patient to care for his daily needs with his unaffected arm

A right hemiplegia in a right-handed person is a serious disability because of the sensory and motor aphasias and the lack of skill in the left hand to perform the activities essential for daily living The training of the left hand should be started early, as the patient must become left handed if he ever hopes to care for his daily needs Simple tasks in eating and dressing should be started Left-handed writing must be practiced, as this is an important means of communication, especially when speech is affected

The Affected Arm and Hand Training of the affected arm is started while the patient is developing one-handed skills with the unaffected arm If the arm is flaccid, a re-education program similar to that used in poliomyelitis should be started Many of these patients have a complete return of function if the muscle re-education is given carefully over a long period of time The rehabilitation of the spastic arm should start at the shoulder The most difficult shoulder movement for the patient to regain is external rotation Flexion and extension of the forearm likewise are difficult for the spastic hemiplegic to perform When asked to flex the elbow, he elevates the shoulder and adducts and internally rotates the arm Pronation and supination of the hand are usually impossible, since these are some of the last movements learned by man and hence the last to return Internal and external rotation of the arm are primitive movements and the patient attempts to substitute these movements for pronation and supination The fingers and thumb are usually flexed tightly If the fingers and thumb are forced open, they can be flexed, but active extension movements are usually impossible

of reducing increased intracranial pressure in the presence of a cyst or tumor is the administration of magnesium sulfate 60 cc of 25 per cent solution given once a day by mouth, or as a rectal retention enema of 120 cc of 50 per cent solution given once a day and held for 30 minutes In the very critical case, where rapid dehydration is imperative to save life, the measures recommended for cerebral edema should be carried out

A common manifestation of increased intracranial pressure is vomiting *nature's method of dehydration This however upsets the elec*trolyte balance leading to alkalosis For these patients parenteral isotonic sodium chloride should be administered subcutaneously or intravenously *or with 5 per cent glucose added Any patient to undergo intracranial* surgery must have fluid and electrolyte balance established in the rest of the body to withstand the anesthesia as well as the surgery Usually 2000 to 3000 cc of intravenous fluid per 24 hours will suffice

Lumbar puncture to relieve increased intracranial pressure in the presence of a space occupying lesion must be done with greatest caution for fear of producing a mechanical shift of intracranial structures that may be detrimental to the patient If it is to be performed, the method as outlined under Cerebral Edema should be used

Inflammation of the Brain

Acute inflammations of the brain include chiefly (1) acute encephali*tis of varied etiology, (2) traumatic encephalitis and (3) suppurative* encephalitis (abscess)

Acute Encephalitis

There is a large group of seemingly heterogeneous causes of acute encephalitis with various classifications The encephalitides have been grouped under virus and non virus etiology primary and secondary according to the locality of an epidemic—St Louis eastern and western equine types Japanese Russian, Australian according to the season of the year in which a type is most prevalent, spring summer summer-autumn and those of irregular seasonal distribution

In this discussion acute encephalitis will be considered (1) as a pri*mary infection of virus origin, and (2) as a post infectious complication* The first group includes epidemic or lethargic encephalitis (von Economo) the Russian St Louis eastern and western equine types

Exercise IV Flexion of forearm and arm of the affected side

Purpose To combine these flexion movements so that the patient may use the hand in daily activities, such as holding paper down while writing

Position Sitting on a chair in front of a table

Instructions The patient flexes the forearm to table level and then flexes the arm so that the forearm rests on the table These movements must be performed without elevating the shoulder or adducting the arm

Repeat five times on the hour

The habit of routinely keeping the hand in the lap interferes with re education It must be placed in the position for finger action

The WRIST, if not flexed, needs no special training There are very few activities which cannot be performed even with a fixed wrist The functional use of the hands has been increased in several young patients with extreme flexion of the wrist by fusing the wrist joint A cock up splint should be used if there is extreme flexion of the wrist and this should be combined with a "pancake" splint if the fingers are tightly flexed

The FINGERS of the spastic hemiplegic patient are most difficult to re educate for any useful purpose If good function is ever attained it represents a great cost in time and concentrated effort by the patient In the aged with advanced cardiovascular disease it is seldom worth the effort One should not, however, have the patient give up hope of ever using the fingers He must be made to understand that the movements of the fingers depend upon the proper functioning of the shoulder, elbow, and hand and the placing of the hand in positions for purposeful move ments Exercise for the fingers should be purposeful and wherever pos sible should be in terms of functional activity in which the patient re learns a practical skill which will prove functionally useful, such as but toning, manipulating zippers, handling objects and self-care activities The following exercises for the fingers can be used for the purpose in dicated

Exercise V Extension of fingers and thumb

Purpose To prevent finger contractures by extension of fingers and thumb

Position Sitting on a chair

Instructions With the fingers of the unaffected hand, extend each finger and the thumb of the affected hand

Repeat five times on the hour

in doses of 0 25 to 0 5 gm by intramuscular injection in severe cases and intravenously in extreme cases should be used In infants the elixir of phenobarbital, 2 0 to 8 0 cc should be given 2 to 4 times a day Another excellent sedative in infants with encephalitis is a 5 5 per cent sugar free elixir of chloral hydrate (Somnos) in doses of 2 0 to 8 0 cc 3 or 4 times a day The bowels should be emptied by enemas and urinary tract infection avoided by urinary antiseptics, such as methenamine mandelate (Mandelamine) Mechanical restraints should never be employed in the treatment of acute encephalitis

Post encephalitic Sequelae

Although some of the encephalitides especially the Russian eastern equine Japanese B Australian X post measles and post vaccinal types, may have extremely variable neurological sequelae from mild to very severe the most common symptom complex to follow encephalitis in adults is *paralysis agitans* This is seen particularly after lethargic encephalitis and influenza It should be treated as described on page 936

In children under 10 years of age the usual complication is a personality change and behavior disorder Nervous residuals occur rarely after the St Louis types and western equine encephalomyelitis For symptoms such as nervousness weakness lethargy stammering and lowered intelligence, which may follow encephalitis there is no available treatment beyond symptomatic measures

Some surgical procedures have been found to be successful in the treatment of certain of the residuals of encephalitis Cortical ablation may be helpful for palsy tremor and athetoid movements but it may also produce considerable disability Unilateral tremor may be helped by section of the pyramidal tract at the level of the second cervical segment Pallido fugal section has been found useful in some instances of tremor but it is applied best to cases of unilateral tremor Such procedures are to be considered only in intractable cases

Suppurative Encephalitis Abscess of the Brain

Brain abscess has its origin in one of 3 ways (1) by direct extension from the middle ear or mastoid or frontal air sinus (2) from penetrating injuries of the skull and (3) metastatic usually from the lung

muscular training There are various grades of palsy, some with minimal handicaps, others hopelessly irreversible It is in the former group that proper evaluation, education at the individual level, and proper perspective can give very encouraging results

Convulsive disorders commonly accompany cerebral spasticity Glutamic acid has been heralded by some as being effective in raising the mental level in some cases It may make the individual appear brighter since the convulsions are better controlled The dosage of glutamic acid for this disorder should be large, 1 0 to 3 0 gm 4 times a day by mouth, preferably before meals Elixir of mephenesin (Tolserol), 0 1 gm per cc, for its curare-like effect, may also be tried for the treatment of the spastic condition, give it in doses of 8 0 to 12 0 cc 3 times a day after meals

Tumors and Cysts of the Brain

In the treatment of tumors and cysts of the brain, proper localization with attempt at removal by a neurosurgeon becomes of paramount importance and is advised

At the same time considerable help can be given by medical means to the patient with a space-occupying lesion Tumors and/or cysts may arise in a silent area of the brain, frontal or pre-temporal lobe regions, giving rise to increased intracranial pressure without any localizing signs The pain of increased intracranial pressure, being due to mechanical pressure, must be treated by removal of the expanding lesion if possible For the pain, acetylsalicylic acid and other salicylate compounds are of no benefit Morphine must not be used, since it will imperil respiration already altered by the increased pressure Also it may increase the pressure already present Codeine phosphate, on the other hand, is the most useful drug for the pain and restlessness, when given in doses of 30 to 60 mg by mouth or hypodermically Methadone in a dose of 5 to 10 mg is also useful in these cases

For the increased intracranial pressure medical dehydration can be used as a temporary expedient until surgical management can be accomplished Great caution must be exercised, however, that the dehydrating measures are not carried to such an extreme degree as to produce a state of toxic dehydration (severe dehydration with electrolyte imbalance), which makes the patient a poor surgical risk The best means

Internal hydrocephalus is frequently an accompaniment of spina bifida, in which the conus medullaris of the cord is anchored in the meningocele at a level lower than the normal The resulting traction on the cord pulls the brain stem and cerebellar tonsils into the foramen magnum giving rise to the Arnold Chiari malformation or other congenital abnormality which in turn gives rise to an obstructive hydrocephalus

In the obstructive form treatment is surgical, the point of obstruction should be located and released if possible If the point of obstruction is inaccessible, the Torkildsen procedure is very useful and consists of the rerouting of fluid from the ventricle by a catheter under the occipital scalp to the cisterna magna The latter procedure is most effective in obstructive tumors and in slowly progressive hydocephalus

In the communicating form coagulation of the choroid plexus may be effective in some instances More recently a technique has been devised utilizing a catheter inserted into the spinal theca in the upper lumbar region *In either type repeated tapping of the ventricles will do no good and will only invite infection*

Epilepsy

Convulsive attacks may result from cerebral disease from general physiological imbalance from poison or they may be produced by no known cause This latter group constitutes the idiopathic epilepsy cases and it is this group which presents an especially difficult therapeutic problem Cerebral lesions such as brain tumors congenital lesions infections, scars and vascular and degenerative diseases producing convulsions can usually be recognized and the attacks disappear when the primary lesion is corrected if this is possible Likewise convulsions resulting from physiological imbalance of calcium oxygen sugar, from nervous or mechanical disturbances or from poisons usually disappear when the initiating cause is corrected or removed

It is essential that all patients with convulsive episodes be studied in *detail before the diagnosis of idiopathic epilepsy is made* These studies should include a thorough medical examination with complete laboratory studies of the blood including a fasting blood sugar spinal fluid and urine examinations, skull x rays and electroencephalogram In some patients cerebral arteriography should be carried out

When the diagnostic studies indicate that the episodes are idiopathic

Japanese B encephalitis, Australian X disease, West Nile encephalitis, and herpes simplex encephalitis The second group includes the acute encephalitis following influenza, measles, variola, vaccination, chicken pox, mumps, infectious mononucleosis, whooping cough, and lymphocytic choriomeningitis At the present time all these forms of encephalitis are generally considered to be due to various types and strains of virus, and because their treatment is similar, they will be considered together

The management of acute encephalitis should consist principally of symptomatic measures At the present time there is no specific treatment for any one of them The sulfonamides, penicillin, streptomycin, and other antibiotics, as tried, have proved of no value Aureomycin, chloramphenicol, and terramycin have been shown to be of some benefit in certain virus infections, they may be tried in the usual doses, but results are not encouraging All of these agents are of benefit, however, in the prevention and treatment of secondary bacterial infections, particularly in the lungs and the urinary tract

From time to time various sera and vaccines have been developed, but they have produced no consistently beneficial results, and so their use is not advised at present The treatment of encephalitis following measles, German measles, variola (smallpox), vaccination, chickenpox, mumps, infectious mononucleosis, and whooping cough should be symptomatic as discussed in the following paragraphs

The use of general measures are of utmost importance through what may be a very stormy course and prolonged convalescence Skillful nursing care, adequate nutrition, fluid balance, and the use of sedatives for restlessness are essential Since the illness may be prolonged, nasal tube feeding for the administration of food and fluids should be used in preference to parenteral fluids and electrolytes This is particularly important for protein At least 3000 calories a day and a high vitamin intake are recommended If the spinal fluid pressure is found to be elevated, repeated spinal punctures or the use of human serum albumin or dextrose solution, as discussed under Cerebral Edema, should be employed For analgesia, codeine phosphate, 15 to 30 mg, or a combination of acetylsalicylic acid, 0 3 to 0 6 gm, and codeine, 15 to 30 mg, will usually suffice The salicylates are very useful since they are antipyretic

For the restlessness so common in the various encephalitides, the barbiturates are very useful Phenobarbital, in doses of 30 mg to 0 1 gm 2 to 4 times a day, should be employed Sodium amobarbital (Amytal),

(Gemonil), methylphenyl ethyl hydantoin (Mesantoin), methylphenylsuccinimide (Milontin), paramethadione (Paradione), phenacemide (Phenurone), primidone (Mysoline) and trimethadione (Tridione) have been found to be useful agents At present, acetazoleamide (Diamox) is showing promise of usefulness The drug selected depends on type of seizure response to therapy, side effect, and toxic effects The safest effective drugs should be used either alone or in combination *What may be satisfactory in one type seizure in one patient may not* be effective in another patient with the same type seizures Certain general patterns of effectiveness are apparent, however, and when followed usually give more prompt and satisfactory results The barbituric acid derivatives phenobarbital mepho barbital, metharbital, primidone and the hydantoins are most useful in treating grand mal attacks The hydantoins and phenacemide are very useful in controlling psycho motor attacks Petit mal seizures respond most satisfactorily to methylpenylsuccinimide paramethadione and trimethadione, with phenobarbital phenacemide and mephobarbital also exerting some control It must be remembered that with the exception of barbituric acid compounds and diphenyl hydantoin most of these drugs are capable of exerting serious toxic effects such as anemia, agranulocytosis, and aplastic anemia

Grand Mal

Phenobarbital given in a dose of 0 1 gm daily, usually at bedtime is effective and in the milder cases with infrequent seizures it alone may suffice The dose can be increased to 0 1 gm 2 or 3 times a day when needed Usually this drug produces little in the way of undesirable effects although occasionally drowsiness or irritability develops and in the rare patient a skin rash may appear Habituation can also occur

Diphenylhydantoin sodium (Dilantin) is more effective than phenobarbital and is the drug of choice in treating the more severe cases It is given in a dose of 0 1 gm by mouth 3 times a day usually before meals with a glass of water It is highly alkaline and may irritate the stomach If this occurs, the drug should be given immediately after meals When the dose of 0 3 gm a day does not control seizures it may be increased by 0 1 gm every 2 weeks until control is secured or until a dose of *0 6 gm daily is reached Few patients can tolerate a dose larger than 0 6* gm a day In certain patients it is desirable to give larger portions of the

The initial phase of the infectious process is a suppurative encephalitis which, if not too severe, tends to encapsulate itself by a progressively increasing wall of gliosis If the increased intracranial pressure does not become too severe, the lesion should be allowed to encapsulate before surgical intervention is carried out This occurs in an average of 21 days from onset During this time adequate antibiotic therapy, depending upon the organism present as isolated from the spinal fluid, should be instituted

When the walling-off process has become complete, the generalized cerebral edema subsides, and the patient's condition begins to stabilize, then surgical intervention with needle or catheter drainage and subsequent irrigation of the cavity should be carried out In some instances the total enucleation of the abscess can be done successfully, particularly in the ones located more superficially During the entire course of treatment the antibiotics should continue to be given in adequate dosage

In abscesses occurring by extension from the mastoid or frontal sinus, the primary, or focus of, infection should be eradicated first In the penetrating wounds of the brain the foreign body material should be removed as soon as possible to prevent abscess formation In the metastatic type the primary focus should be determined and eradicated to prevent other abscesses from occurring

Hydrocephalus

Internal hydrocephalus is the accumulation of excessive cerebrospinal fluid owing to an imbalance between its formation by the choroid plexus and its re-absorption by the Pacchionian granulation system Two types are generally recognized (1) obstructive, and (2) non-obstructive or communicating Recent work disclosing a variety of pathological lesions productive of hydrocephalus have a single feature in common—namely, all lesions create an obstruction at some point in the pathway of cerebrospinal fluid flow In the obstructive type, which is by far the most common, the point of obstruction has been found to involve most commonly the cerebral aqueduct and the recesses about the fourth ventricle Hydrocephalus secondary to an inflammatory process, such as meningitis, is due to a plastic exudate about the recesses of the fourth ventricle and may have, in addition, scarring of the Pacchionian bodies, thereby making normal absorption impossible In the communicating type the fibrosis of the Pacchionian bodies may be the only evident finding

Mephobarbital (Mebaral), 0 2 gm 1 to 3 times a day by mouth may be used as a substitute for phenobarbital It gives undesirable side reactions in some patients, and this makes it a less satisfactory drug than phenobarbital

Primidone (Mysoline) 0 25 gm daily increased gradually by increments of 0 25 gm at weekly intervals may be tried until convulsions are controlled, or until the total daily dose has reached *1 5 gm*, or toxic effects such as vertigo nausea vomiting drowsiness, dysarthria ataxia skin rash, or pitting edema of legs appear In children up to 8 years the initial dose should be 0 125 gm and increments should be on this basis with a total daily dose being approximately one half the adult dose Occasionally primidone will control attacks when other treatment fails For the most part it has approximately the same therapeutic effect as phenobarbital Frequently following the initial dosage there is nausea and vomiting If one waits a day or two the drug usually can be resumed without this toxic effect recurring

Metharbital (Gemonil) another barbiturate derivative is also an effective agent which may control seizures when other agents fail It seems to be effective in patients where seizures result from organic brain damage It is less sedative than phenobarbital and very few untoward *effects are observed from its administration* A dose of 0 1 gm 1 to 3 times daily for adults and 0 05 gm 1 to 3 times daily for infants and children is recommended The dose may be increased to secure more complete control until minor toxic effects such as irritability dizziness, gastric distress drowsiness, or skin rashes appear It is very useful in combination with other non barbiturate agents

Acetazoleamide (Diamox) has occasionally proved effective in supressing seizures when other agents have been unsatisfactory or have failed It should be given in a daily dose of 0 25 to 0 5 gm It can be used in conjunction with other agents Toxic effects are minimal but an occasional allergic reaction, tingling of extremities, and even dis orientation has occured Sufficient data has not accumulated as yet to assign this versatile agent its definite role in the treatment of seizures Prolonged daily administration may be toxic and there is evidence accummulating which indicates that tolerance and resistance to its effect develops

The bromides are no longer used to any great extent because of their tendency to produce undesirable side effects The danger of bromidism is always present and changes in diet and hydration and many other fac-

in nature, treatment directed toward their suppression should be started The type of convulsive episode, whether grand mal, petit mal, Jacksonian or psychomotor attacks, determines for the most part the choice of therapy, but certain general measures are applicable to all of them. These patients should avoid mental or physical strain, secure adequate rest, and arrange to live a well-regulated, pleasant, but not sedentary life A moderate amount of physical exertion and outdoor activity is desirable For vigorous individuals active physical exercise such as tennis, golf, and manual labor is desirable Overeating should be avoided and the bowels kept well-regulated An acid-ash diet with ample fluid intake, with care taken to avoid excess, is recommended by many Alcohol in all forms is harmful and may produce seizures When constipation is present, it should be treated

These patients should be taught and be expected to live a nearly normal life School, work, and play should be continued as normally as possible Occupations and activities such as automobile driving, horseback riding, swimming, and other sports likely to be dangerous should a convulsive attack occur are better changed for those with little or no hazard, but above all the patient must be kept in normal active channels

Proper mental hygiene, preferably supervised by a psychiatrist, is most helpful These patients must be aided in overcoming any sense of inferiority and should be urged to participate in social activities such as dances, parties, and community gatherings Psychotherapy is frequently a most helpful adjunct in treatment

Diet Formerly there was considerable enthusiasm for dietary measures in the control of epilepsy Fasting has long been known to be beneficial and, when food is withheld for several days, attacks may cease or become much less frequent This beneficial effect is produced by the ketosis which results from the fasting Later the ketogenic diet was developed, and a few years ago it was very popular At the present time this diet, as well as the dehydration regime and the acid ash diet, has been replaced by the more effective, and certainly more easily managed, anticonvulsant drug therapy It has limited use in children, but in them, too, suppressive drug therapy is more effective and easier to manage

Anticonvulsant Drugs Drug therapy for the treatment of epilepsy was initiated by the introduction of bromide in 1857 This was followed by phenobarbital in 1912 and diphenylhydantoin sodium (Dilantin) in 1939 In more recent years mephobarbital (Mebaral), metharbital

helpful, and if grand mal seizures are also present, the combination is especially beneficial If necessary it may be combined effectively with diphenylhydantoin sodium

Paramethadione (Paradione), 0 3 to 2 0 gm daily, may be substituted for trimethadione It is more effective than trimethadione against major seizures and therefore more desirable than trimethadione as a combination with diphenylhydantoin in the treatment of major seizures It is capable of producing toxic effects similar to those of trimethadione and therefore the same precautionary measures as recommended for trimethadione must be observed Generally it is not as effective as trimethadione which should be tried first On the other hand, it may be more effective than trimethadione in some cases

Patients not responding well to the above drugs should be tried on methylphenylsuccinimide (Milontin) 0 5 to 1 0 gm 3 times a day increased by increments of 0 5 gm a day at two week intervals until seizures are controlled or a maximal dose of 5 0 gm daily is attained Usually a daily dose of 2 0 to 3 0 gms is satisfactory Infants should receive 0 5 gms daily children up to age 4 years 1 to 2 gms from ages 4 to 9 years 2 gms Although toxic effects are not usually serious careful observation must be maintained for excessive sedation, ataxia, emotional changes rashes and urinary abnormalities Microscopic hematuria and signs of renal damage may appear but will frequently clear if the dose is lowered

An occasional patient with petit mal is effectively controlled with phenacemide (Phenurone) It however is less active than the above drugs and unfortunately has serious toxic properties For these reasons it should be used only when other agents are not giving satisfactory results The dose and method of administration is the same as described for it under psychomotor epilepsy

Jacksonian Seizures

Treatment for these attacks is similar to that described for Grand Mal The initiating lesion should be located and corrected by surgery whenever possible

Psychomotor Attacks

The least toxic and highly effective diphenylhydantoin (Dilantin)

dose at special times For example, patients subject to nocturnal seizures are better controlled if a large portion of the daily dose is given at bed time Children under 5 years of age should be started on 0 03 gm by mouth twice a day If a larger dose is required and the drug is tolerated, it may be increased to 0 03 gm 3 or 4 times a day The drug should be given with milk or cream to prevent stomach irritation For children over the age of 5 years a dose of 0 1 gm 3 times a day, increased to 0 1 gm 4 times a day when necessary, is usually satisfactory Children must be watched carefully, and the dosage altered if toxic signs appear

To prevent the hyperplasia of the gums that occurs not infrequently after the use of diphenylhydantoin, the patient should be instructed to brush his teeth thoroughly twice a day, including thorough massage of the gums, and to visit the dentist at least every 3 months to receive dental hygiene

The combination of diphenylhydantoin sodium with phenobarbital is more effective than either of the drugs used singly It is usually possible to use a smaller dose of each Diphenylhydantoin sodium (Dilantin), 0 3 to 0 4 gm, combined with phenobarbital, 0 1 to 0 2 gm, by mouth daily is effective and is usually better than either drug used alone in larger dosage

Patients receiving diphenylhydantoin may show various toxic signs such as dizziness, ataxia, blurring of vision, nervousness, fatigue, head aches, insomnia, irritability, gastric irritation, morbilliform skin erup tions, and hyperplasia of the gums

The drug must be discontinued immediately if purpura, skin rash, or drug fever appears Mild side reactions, such as hyperplasia of the gums, do not require cessation of treatment If nausea and vomiting ap pear as a result of severe gastric irritation, relief is occasionally afforded by the administration of 1 or 2 cc of dilute hydrochloric acid, taken in half a glass of water through a drinking tube or straw at the time the drug is given Chlorpromazine in doses of 25 to 50 mg may be tried

Methylphenylethyl hydantoin (Mesantoin) is an effective agent that has a similar action and can be substituted for diphenylhydantoin sodium, but unfortunately in the occasional patient it exerts a highly toxic effect on bone marrow, resulting in aplastic anemia In view of this serious complication the drug should be used with great caution Blood studies, including white blood cell counts, and smears should be done at 2- to 4-week intervals The initial dose is 0 3 gm daily, increased grad ually to 0 9 gm daily

brain tumor, syphilis, acromegaly, or functional mental disease Usually the attacks are effectively controlled by amphetamine (Benzedrine) sulfate, 10 mg by mouth 3 times a day Occasionally a larger dose is necessary, but care must be taken to avoid hypertension tachycardia, and excessive nervousness The dextro-rotary form of amphetamine sulfate is also effective and may be used in the same dosage as amphetamine It has approximately the same toxic properties as amphetamine.

Methamphetamin (Desoxyephedrine) hydrochloride is also useful It appears to have a slightly greater central stimulating effect and possibly less circulatory effect A dose of 2 5 to 5 mg by mouth, gradually increased to 2 or 3 times a day as needed, is recommended Toxic effects are the same as those found from the use of amphetamine and when they appear, the dose should be reduced

These patients should secure longer hours of rest at night and avoid overeating, overheating, mental strain, and monotonous tasks when possible Psychotherapy and an active interesting program of activities are definitely helpful

Diseases of the Dura Mater

Pachymeningitis

Usually this is an extension from pyogenic, tuberculous, or syphilitic disease of adjacent bones, and there may be cerebral and spinal forms and both external and internal pachymeningitis Their treatment should be that appropriate to the possible etiology of bone diseases mentioned above If the diseased bone which has started the process undergoes necrosis, surgical removal of these parts of it will be necessary

Subdural Hematoma

Surgical exploration with removal of the hematoma should be the method of treatment

Diseases of the Arachnoid and Pia Mater (Leptomeninges)

Leptomeningitis Meningitis Arachnoiditis

An acute inflammatory process of the arachnoid and pia mater should receive the therapy effective against the causative organism as already

tors lead to irregular action A dose of 0 6 to 1 0 gm of the sodium or potassium salt 3 times a day is satisfactory When desired, a more effective concentration can be attained by restricting the sodium chloride intake

How long the use of these anticonvulsant drugs should be continued after seizures cease will always be a problem A period of at least 2 years seems reasonable Some believe that they should be continued until an electroencephalogram shows a very distinct return toward normal as compared with one taken before anticonvulsants were begun A gradual decrease in size and frequency of doses of anticonvulsants is advised, and repeated electroencephalograms should be taken to see whether abnormality has returned or increased If abnormalities remain, anticonvulsants should be again increased to the dosage that has been found effective for the patient

Once commenced, medication should be changed gradually as needed but sudden reduction in dosage must be avoided When one drug is substituted for another, the new drug should be gradually increased until the optimum dosage is attained and then the previous drug gradually decreased in amount until it is discontinued Once satisfactory results are secured with a drug or a combination of drugs, a great effort should be made to maintain the status quo Many patients are maintained for years on the same dosage

Petit Mal

If attacks are mild and infrequent, no medication may be required. More severe infrequent attacks often respond to phenobarbital, 0 1 gm. daily, usually this should be given at bedtime Patients with frequent or more incapacitating seizures should be given trimethadione (Tridione), 0 3 gm daily If necessary, the dose may be increased to 1 0 to 2 0 gm daily until attacks are controlled or toxic symptoms appear Because the drug is capable of producing blood destruction, nephrosis, hepatitis, and other toxic reactions, patients with a history of blood dyscrasia or liver or kidney disease should not receive this therapy All patients who are being given trimethadione should have their blood and urine examined at least once a month If any abnormalities appear, the drug should be stopped Sudden withdrawal of this drug does not precipitate seizures Combination of trimethadione with phenobarbital is

8 KOZOL H L Mesantoin in Treatment of Epilepsy Report on 200 Patients under Treatment for Periods Ranging from Two Months to Four Years *Arch Neurol and Psychiat* 1950 LXIII p 235
9 LENNOX W G Tridione in the Treatment of Epilepsy *Jour Amer Med Assoc*, 1947 CXXXIV p 138
10 LIVINGSTON S and KAJDI L Use of Phenurone in Treatment of Epilepsy *J Pediat*, 1950 XXXVI p 159
11 MERRITT H H and CARTER S Anticonvulsant Drugs *Med Clinic No Amer*, March 1950 p 341
12 MUSTARD H S and LIVINGSTON S Tridione Therapy in Epilepsy Review of Results in 156 Patients with Petit Mal Epilepsy with Special Reference to Side Reactions *J Pediat* 1949 XXXV p 540
13 NIELSEN J M *Agnosia, Apraxia Aphasia*, Paul B Hoeber Inc 1946
14 MILLIKAN C H SIEKERT R G and SHICK R M Studies in Cerebrovascular Disease I The Syndrome of Intermittent Insufficiency of the Basilar Arterial System II Some Clinical Aspects of Thrombosis of the Basilar Artery III The Use of Anticoagulant Drugs in the Treatment of Insufficiency or Thrombosis within the Basilar Arterial System *Proc Staff Meet Mayo Clinic* 1955 XXX 61 93 116
15 KRUESI O R and SCHILLING F J The Clinical Evaluation of Phenylindandione as an Anticoagulant *New Eng Jour Med* 1954 CCLI 927
16 RUSK H A Outline of Hemiplegia and Rehabilitation, *Inst of Phys Med* N Y University Bellevue Medical Center
17 FORSTER R M Medical Therapy of Epilepsy *Neurology* 1951 I 153
18 TOMAN J E P Neuropharmacologic Considerations in Psychic Seizures *Neurology* 1951 I 444

sodium administered in the same dose and manner as for grand mal attacks is recommended for psychomotor attacks If it is not effective and the seizures are serious and when the patient can be followed adequately, a combination of Mesantoin (0 1 gm) and Phenobarbital (0 015 gm) (Hydantol), 1 tablet 2 to 4 times a day, or phenacemide (Phenurone), 0 5 to 1 0 gm 3 times a day for adults, usually is effective For children 5 to 10 years of age approximately one half these doses should be used Phenacemide is especially valuable if temporal lobe focal seizures are present Patients on the drug must be observed carefully and repeated blood studies are necessary since it can cause agranulocytosis Other toxic effects are hepatitis, disturbances in personality, especially depression, and skin rashes Methyl phenylethylhydantoin (Mesantoin), paramethadione (Paradione), and trimethadione (Tridione) also exert beneficial effects and should be tried in cases not responding properly to exhibiting toxic effects from phenacemide The same dose and precautions as recommended for petit mal are to be followed

Status Epilepticus

Treatment must be prompt and vigorous Phenobarbital sodium, 0.4 to 0 8 gm intravenously, or paraldehyde, 1 to 6 cc intravenously, is frequently effective Severe attacks may be relieved at times by general anesthesia with ether Tribromoethanol (Avertin), 0 075 mg per kilogram of body weight given by rectum, is also useful in controlling these seizures Anesthesia with intravenous sodium pentothal will also be effective

Management of the Seizure

During a grand mal attack the patient must be protected from injury Constricting clothing should be loosened, and the tongue should be protected by the insertion of a padded throat stick or other stock material between the teeth Parenteral fluids and nourishment by nasal tube are indicated when attacks are prolonged Care must be exercised to prevent aspiration of food, exposure, and too deep sedation After the attack the patient should be placed in bed and permitted to sleep and rest until he feels normal once more

Narcolepsy

These patients should be thoroughly studied for the possibility of

8 KOZOL H L Mesantoin in Treatment of Epilepsy Report on 200 Patients under Treatment for Periods Ranging from Two Months to Four Years *Arch Neurol and Psychiat* 1950 LXIII p 235
9 LENNOX W G Tridione in the Treatment of Epilepsy *Jour Amer Med Assoc*, 1947 CXXXIV p 138
10 LIVINGSTON S and KAJDI L Use of Phenurone in Treatment of Epilepsy *J Pediat*, 1950 XXXVI p 159
11 MERRITT H H and CARTER S Anticonvulsant Drugs *Med Clinic No Amer*, March 1950 p 341
12 MUSTARD H S and LIVINGSTON S Tridione Therapy in Epilepsy Review of Results in 156 Patients with Petit Mal Epilepsy with Special Reference to Side Reactions *J Pediat* 1949 XXXV p 540
13 NIELSEN J M *Agnosia, Apraxia Aphasia*, Paul B Hoeber Inc 1946
14 MILLIKAN C H SIEKERT R G and SHICK R M Studies in Cerebrovascular Disease I The Syndrome of Intermittent Insufficiency of the Basilar Arterial System II Some Clinical Aspects of Thrombosis of the Basilar Artery III The Use of Anticoagulant Drugs in the Treatment of Insufficiency or Thrombosis within the Basilar Arterial System *Proc Staff Meet Mayo Clinic* 1955 XXX, 61 93 116
15 KRUESI O R and SCHILLING F J The Clinical Evaluation of Phenylindandione as an Anticoagulant *New Eng Jour Med* 1954 CCLI 927
16 RUSK H A Outline of Hemiplegia and Rehabilitation, *Inst of Phys Med* N Y University Bellevue Medical Center
17 FORSTER R M Medical Therapy of Epilepsy *Neurology* 1951 I 153
18 TOMAN J E P Neuropharmacologic Considerations in Psychic Seizures *Neurology* 1951 I 444.

discussed under respective subheadings of Infectious Diseases With the present availability of various sulfonamides and antibiotics, the former use of specific antisera has been given up, and thus has greatly simplified treatment, although repeated lumbar puncture still remains with a few exceptions a necessary part of treatment

Chronic forms of meningitis occur, usually tuberculous or syphilitic. These should be treated in accord with the etiology as described else where under Tuberculosis and Syphilis Chronic arachnoiditis has been given various names, such as *arachnoiditis serosa, circumscripta serosa* or *cystica, diffuse proliferative* or *hypertrophica,* and is recognized by x-ray after the injection of a radio-opaque substance, treatment should be surgical

Meningismus Meningism

Lumbar puncture should usually be done for both diagnosis and treat ment This failing, an intravenous injection of hypertonic salt solu tion should be used Only rarely, when localized pressure symptoms persist, is surgical exploration and drainage of pocketed off fluid nec essary

BIBLIOGRAPHY

Diseases of the Brain and Meninges

1 ABBOTT J A, and SCHWAB, R S 'Serious Side Effects of Newer Antiepileptic Drugs Their Control and Prevention" *N E J Med*, 1950 CCXLII, p 943

DENNY-BROWN D "The Treatment of Recurrent Cerebrovascular Symptoms and the Question of 'Vasospasm," *Med Clinic No Amer*, 1951, XXXV, p 1457

3 EDITORIAL The Question of Cerebral Angiospasm," *Ann Int Med*, 1952, XXXVI, p 1129

4 FOLEY, W T, and WRIGHT I S The Treatment of Cerebral Thrombosis and Embolism with Anticoagulant Drugs Preliminary Observations," *Med Clinic No Amer*, May 1950, p 909

5 FORSTER F M and BORKOWSKI, W J "Paradione in Treat ment of Petit Mal Epilepsy," *Am Pract*, 1950, L p 406

6 GRINKER R R, and BUCY, P C *Neurology*, Charles C. Thomas, Springfield, 1949

7 KAUFMAN, I C 'Treatment of Seizures," *Med Clinic No Amer*, September 1950, p 1507

CHAPTER LXXVI (*continued*)

DISEASES OF THE BRAIN AND MENINGES

Headache Migraine

Among the most grateful patients is the individual who is relieved of plaguing headaches Although headache is one of the most common of symptoms if it is not relieved readily by aspirin the physician tends to overlook it or tries to avoid treating it Yet when adequately gone into the proper treatment of a headache can give very gratifying results

Headache is one of the few pains in the body that does not necessarily indicate presence of pathology Except for space occupying lesions or acute inflammations of the meninges or about the head such as sinusitis the great majority of headaches are on a muscular tension or a vascular basis

Tension Headaches

Muscular contraction of the face scalp or cervical area a common consequence of various nervous and emotional tension states and probably accompanied by some vasoconstriction of cranial arteries is often the cause of daily recurrent headaches Usually these are located in the occipital or temporal areas and frequently develop during the day rising to a peak in the early evening This type of headache may also be observed following trauma infection tumors, or metabolic diseases which through involvement of the eye ear nose sinuses skull cervical spine teeth or throat create sustained muscle contraction

As promptly as possible the underlying diseased condition if amenable to treatment should be corrected Immediate release of muscle contraction frequently gives prompt and dramatic relief Help may be obtained in severe cases by the intravenous injection of 0 2 to 0 5 gm of sodium pentobarbital (Nembutal) or sodium amobarbital (Amytal) These drugs may be used in the same dose orally but the benefit may not be so satisfactory Aspirin 0 3 to 0 6 gm given at the same time is also helpful

discussed under respective subheadings of Infectious Diseases With the present availability of various sulfonamides and antibiotics, the former use of specific antisera has been given up, and this has greatly simplified treatment, although repeated lumbar puncture still remains with a few exceptions a necessary part of treatment

Chronic forms of meningitis occur, usually tuberculous or syphilitic These should be treated in accord with the etiology as described elsewhere under Tuberculosis and Syphilis Chronic arachnoiditis has been given various names, such as *arachnoiditis serosa, circumscripta serosa* or *cystica, diffuse proliferative* or *hypertrophica*, and is recognized by x-ray after the injection of a radio-opaque substance, treatment should be surgical

Meningismus Meningism

Lumbar puncture should usually be done for both diagnosis and treatment This failing, an intravenous injection of hypertonic salt solution should be used Only rarely, when localized pressure symptoms persist, is surgical exploration and drainage of pocketed off fluid necessary

BIBLIOGRAPHY

Diseases of the Brain and Meninges

1 ABBOTT, J A, and SCHWAB, R S 'Serious Side Effects of Newer Antiepileptic Drugs Their Control and Prevention," *N E J Med*, 1950, CCXLII p 943

DENNY-BROWN, D The Treatment of Recurrent Cerebrovascular Symptoms and the Question of 'Vasospasm,' *Med Clinic No Amer*, 1951, XXXV, p 1457

3 EDITORIAL "The Question of Cerebral Angiospasm,' *Ann Int Med*, 1952, XXXVI, p 1129

4 FOLEY, W T, and WRIGHT, I S "The Treatment of Cerebral Thrombosis and Embolism with Anticoagulant Drugs Preliminary Observations" *Med Clinic No Amer*, May 1950 p 909

5 FORSTER F M, and BORKOWSKI, W J Paradione in Treatment of Petit Mal Epilepsy, *Am Pract*, 1950 L p 406

6 GRINKER, R. R and BUCY, P C. *Neurology*, Charles C. Thomas, Springfield, 1949

7 KAUFMAN I C "Treatment of Seizures' *Med Clinic No Amer*, September 1950 p 1507

CHAPTER LXXVI (continued)

DISEASES OF THE BRAIN AND MENINGES

Headache Migraine

Among the most grateful patients is the individual who is relieved of plaguing headaches Although headache is one of the most common of symptoms, if it is not relieved readily by aspirin the physician tends to overlook it or tries to avoid treating it Yet when adequately gone into the proper treatment of a headache can give very gratifying results

Headache is one of the few pains in the body that does not necessarily indicate presence of pathology Except for space occupying lesions or acute inflammations of the meninges or about the head such as sinusitis the great majority of headaches are on a muscular tension or a vascular basis

Tension Headaches

Muscular contraction of the face scalp or cervical area a common consequence of various nervous and emotional tension states and probably accompanied by some vasoconstriction of cranial arteries is often the cause of daily recurrent headaches Usually these are located in the occipital or temporal areas and frequently develop during the day rising to a peak in the early evening This type of headache may also be observed following trauma infection tumors or metabolic diseases which, through involvement of the eye ear nose sinuses skull cervical spine teeth or throat create sustained muscle contraction

As promptly as possible the underlying diseased condition if amenable to treatment should be corrected Immediate release of muscle contraction frequently gives prompt and dramatic relief Help may be obtained in severe cases by the intravenous injection of 0 2 to 0 5 gm of sodium pentobarbital (Nembutal) or sodium amobarbital (Amytal) These drugs may be used in the same dose orally but the benefit may not be so satisfactory Aspirin 0 3 to 0 6 gm given at the same time is also helpful

Before beginning definitive therapy it is well to establish the presence of a migraine mechanism For the classical syndrome of aura unilateral headache nausea and vomiting the test described may not be necessary But with the broader concept a reproduction of the patient s symptoms not only is confirmatory it establishes for the physician the fact that the underlying disorder is vascular and most important it gives to the patient a confidence that reproducibility denotes understanding The test consists of the sublingual administration of nitroglycerine With the patient lying comfortably and without a headache record the pulse and blood pressure and then give 1 2 mg (2 of the 0 6 mg hypodermic tablets) sublingually In one to three minutes the patient will usually remark I am getting a headache this is most often mild The pulse should accelerate 5 to 15 beats and usually the blood pressure falls 10 to 20 mm of mercury The diagnosis rests not with the fact that a headache has been produced for nitroglycerine in such doses will give a headache to many individuals but with the fact that the headache appears in the same location and is of the same character but less in degree as the headache of which the patient complains It does not require the full reproduction of the headache to make the diagnosis Occasionally an hour or two after the test the patient may experience one of his severe migraine headaches Frequently this may be avoided by using only 0 4 to 0 6 mg of nitroglycerine in patients with hypertension or hypotension

After another minute or two when the reproduced headache has reached its peak prompt relief will usually be obtained by pressure on one or the other carotid artery (not carotid sinus pressure) for frontal or temporal ache on either side or the occipital arteries for occipital headache as the case may be In addition the patient may be given one or two tablets containing ergotamine tartrate 1 mg and caffeine 100 mg (Cafergot) by mouth for further vasoconstricting effect

If no headache is produced the test is negative For reasons not well understood even in a classical case the test may be negative on the first trial and strongly positive on a second trial a day or two later It is of no value if done when the patient has one of his usual headaches

In beginning the treatment of a patient with migraine headaches the success of the therapy is directly proportional to the enthusiasm of the physician It is well to instruct the patient in the mechanism of the attacks early during therapy that is vasoconstriction in the aura vasodilatation during the headache The demonstration of a headache with the nitroglycerine test or a histamine test in the case of histamine cephal

Application of heat, in the form of hot tub baths, hot towels, packs, lamps, or electric hot pads to the contracted muscle for 15 to 30 minutes daily, is often soothing and frequently rapidly relieves the pain Occasionally, gentle massage with a soothing analgesic lotion, such as methyl salicylate (oil of wintergreen) or chloroform liniment, relieves muscle irritability and with it the headache

These patients are usually tense and irritable, and have difficulty in relaxing Mild daily sedation for brief periods with phenobarbital, 15 to 30 mg after meals and at bedtime, while the patient is receiving more definitive treatment, is often useful in preventing or reducing the severity of the pain

Migraine

The usual concept of migraine, with its periodicity, scotomata, hemicrania, nausea, and vomiting, must be broadened Migraine is a mechanism, not a disease As a mechanism, the patient must be considered to have a migraine diathesis, in whom any number of precipitating factors can cause a headache The ache is due to distortion, usually dilatation of extracranial dural, basilar, or vertebral arteries and their branches Anything that produces sudden vasodilatation of these vessels in a susceptible individual will produce a headache The more common causes include nervous tension, emotional upsets fatigue, relaxation (the cause of morning headaches, particularly Sunday morning), toxic reactions to food substances, premenstrual tension, and drugs Among foods the common offenders are coffee, chocolate beans, dairy products, nuts, and sometimes beef and pork Allergy in the usual sense is not apparent in these patients—that is, they practically never have a past history of hay fever, asthma, hives, and so on With chocolate the headache is likely to occur after only a few hours, with coffee it is a matter of accumulation the ache occurring after the person has drunk coffee regularly for 5 to 7 days Sometimes when coffee causes migraine, the individual can tolerate black coffee but the addition of cream may precipitate an ache

Conversely, since vasodilatation causes the headache, a drug such as ergotamine that will reduce rapidly the calibre of the involved vessels toward normal ordinarily will alleviate the headache Salicylates and opiates are consequently frequently unsuccessful since they have no effect on the altered vascularity The latter also do not influence the perivascular edema of the brain that occurs after a migraine headache has been present for more than one or two days

and sedative drugs used in the further relief of symptoms Further if the headache is not relieved completely aspirin 0 3 to 0 6 gm will often eliminate the ache whereas previously it has usually been ineffective By a method of trial and error it may be found that in the case of rapid onset of headache which tends to recur an hour or two after sublingual ergotamine the administration of two Cafergot tablets swallowed after the sublingual tablets have dissolved will prevent the recurrence

For the patient with a headache already under way for a short time ergotamine tartrate (Gynergen) 0 25 mg subcutaneously should be given, if the first dose is tolerated and a second is needed in one or two hours 0 5 mg may be given subcutaneously No more than 1 0 mg should be given in 24 hours Dihydroergotamine (DHE 45) 1 0 cc intravenously or intramuscularly can be used if a milder drug is neces sary it acts rapidly and is usually effective With a headache present the inhalation of 90 per cent oxygen by face mask can also be effective since it is a mild vasoconstrictor

If the ergot preparations cause too severe reactions isometheptene (Octin) 0 1 to 0 2 gm subcutaneously or by mouth as isometheptene mucate 0 13 gm at onset may be effective in the milder cases it is often ineffective in severe migraine headaches

Some individuals can tell the night before that they will have a head ache on awakening the next morning In such instances the oral use of one or two Cafergot tablets at bedtime or the insertion of a Cafergot suppository (EC 110) containing ergotamine tartrate 2 mg plus caf feine 100 mg on retiring may prevent the headache A Cafergot sup pository can cause just as much nausea and vomiting as the oral tablet but this also can be avoided by taking atropine sulfate 0 4 mg or chlor promazine 10 to 25 mg by mouth The following suppository is excel lent and there is less tendency for nausea or vomiting to occur following its use

Ergotamine tartrate	2 0 mg
Caffeine	100 0 mg
Bellafoline	25 mg
Sodium pentobarbital	60 0 mg

Make up in cocoa butter base #15

gia, is quite convincing Next, a plan of study should be instituted with the patient to ferret out precipitating factors or substances This has the advantage of making the patient help to work out his own problem Among other features in the examination, special attention should be paid to the frequency of the headaches, for here treatment differs—the time of day, rapidity of onset, duration, and any factors that have been found to give relief

A most common denominator in migraine headaches is nervous tension This is particularly true when headaches occur three and four times a week, or even daily For this a basic sedative, such as pentobarbital (Nembutal) 0 049 gm, three or four times a day has been found very useful For vascular headaches that are almost daily and on a nervous tension basis, potassium thiocyanate as used for hypertensive headaches is useful A mixture of equal parts of Elixir Potassium Thiocyanate and Elixir Phenobarbital, one teaspoonful three or four times a day, has been found to be very effective and almost devoid of thiocyanate reactions If this preparation is used, checks of blood thiocyanate level should be made as is recommended when the drug is used in the treatment of hypertension

Anemia should be carefully watched for, since its presence can significantly increase the frequency and intensity of vascular headaches When present, it should be adequately treated as discussed in Part XVI, Chapter LI, page 623

Another often overlooked factor in frequently recurring migraine is the presence of impacted lower molar teeth These should always be looked for and removed when necessary

For the acute attack at less frequent intervals, many ergot preparations are available With all of them the best results are obtained by giving the effective dose at the very onset of an attack For the patient whose migraine headache requires one to five hours in building up, ergotamine tartrate 1 mg plus caffeine 100 mg (Cafergot), 2 to 4 tablets by mouth at the onset is frequently effective If only 15 to 30 minutes are required, ergotamine tartrate 1 0 mg tablets, 2 to 4 given sublingually, often prove more effective than the mixture If either of these ergot preparations causes nausea and vomiting atrophine sulfate 0 5 mg, or chlorpromazine (Thorazine) 10 to 25 mg, given with the ergotamine by mouth is frequently useful Chlorpromazine is also highly effective in suppressing the nausea and vomiting produced by the migraine itself Indeed the drug does much to relieve the distress of the attack It calms the patient, relieves nausea and vomiting, and may potentiate analgesic

as having much pain A method that may be used to determine the severity of the headache is to give up to 0 2 gm sodium amobarbital (Amytal) in 3 cc distilled water slowly intravenously until the patient obtains relief One begins with a syringe containing 0 3 gm in 5 cc distilled water and increments of 30 mg (½ cc) are injected intra venously at 5 minute intervals Frequently a very small amount will suffice to bring about relief 30 to 100 mg is usually sufficient and such dosage is not enough to produce significant stupor or sleep Occasion ally as much as 0 2 gm (3 cc) is necessary The relief may last from hours to days Such relief of pain according to Susselman *et al* gener ally means that the headache is of psychic origin organic pain is not so easily relieved When such a mechanism becomes established for the headaches further therapy should be carried out by a competent psy chi atrist

An occasional case with daily headaches even when the histamine test as discussed farther on or the nitroglycerine test already described is negative may be helped by hi tamine phosphate injections 7 to 10 intravenous injections of histamine phosphate are given daily and a total of 2 75 mg in 250 cc physiological saline is administered intra venously during 6 to 8 hours Experience has shown that the infusions are tolerated better each day in the course of treatment so one need not change the dose as is done in desensitization procedures for allergy If a good response is obtained by the intravenous method the patient should be followed in the office and 0 275 mg (1 cc) histamine injected sub cutaneously 3 times a week for 2 or 3 months If the subcutaneous-injection method is not followed through relapse is very likely to occur Such subcutaneous injections can be continued for months if necessary 1 to 3 times a week as the situation demands

Psychotherapy

Since emotional tension and stress are so common as precipitating factors in vascular headaches the physician patient relationship is very important in the ventilation of emotional conflicts and in attempts to manipulate the environment In the latter one must recognize the patient s capacity or lack of capacity to correct tensions or conflicts at work at home or in his social life In any attempt to change the

All ergot preparations should be used very cautiously, or not at all, in organic cardiac disease, angina pectoris, hypertension, obliterative vascular disease, hepatic disease, pregnancy, and septic states associated with intravascular foci

Physical agents, such as rather marked heat or cold, both of which produce vasoconstriction applied to the part of the head involved can aid in alleviating aches For those patients whose headaches are chiefly occipital a quart jar filled with chipped ice, wrapped in a towel, and placed behind the neck while recumbent, produces vasoconstriction by both pressure and cold, and will often give relief within a few minutes

In a few cases, in spite of these measures, the headache will persist for 3 to 5 days, although vasodilatation will for the most part have disappeared In these patients perivascular edema of the brain has occurred and it is causing the persistence of the headache In such instances an adequate analgesic for pain and a soporific to cause sleep will give the best results A combination of Empirin compound with codeine phosphate 15 mg and a quick-acting capsule of secobarbital (Seconal) sodium 0 1 gm, is often effective Other preparations embracing the same principle will work just as well

In rare cases vasodilators, such as nicotinic acid, 50 mg 2 or 3 times a day may be very useful in the treatment of vascular headaches

Prophylaxis

Often a regimen to abort an oncoming headache can be worked out quite satisfactorily for the individual patient, much more difficult to achieve is the formulation of a program to prevent attacks Obviously the discovery of the offending agent or substance and its elimination will be the best prophylactic Where nervous tension plays an important part in causation, the use of a basic sedative temporarily such as phenobarbital, 15 to 30 mg 2 or 3 times daily is frequently effective

Continuous Headaches of Psychogenic Origin

There is a small percentage of patients who exhibit headaches of probably vascular origin that are continuous and fail to respond to any reasonable treatment Often such patients do not impress the physician

of Horton Histamine diphosphate 0 275 mg per cc (1 0 cc equals 0 1 mg histamine base) is used somewhat as follows

1st dose 0 25 cc
2nd dose 0 30 cc
3rd dose 0 35 cc
4th dose 0 40 cc
5th dose 0 45 cc
6th dose 0 50 cc
7th dose 0 55 cc
8th dose 0 60 cc
9th dose 0 65 cc
10th dose 0 70 cc
11th dose 0 75 cc
12th dose 0 80 cc
13th dose 0 85 cc
14th dose 0 90 cc
15th dose 0 95 cc
16th dose 1 00 cc
17th dose 1 00 cc
18th dose 1 00 cc
19th dose 1 00 cc
20th dose 1 00 cc

The first and second doses are administered on the first day and the subsequent doses are administered 2 per day for 10 days Two injections per day may be continued for as long as 2 to 3 weeks If untoward flushing of the face occurs the succeeding dose may reduced by 50 per cent then gradually increased It is advised that maintenance doses *of 1 0 cc (0 275 mg histamine) be given subcutaneously 2 to 3 times* a week after the course suggested above for a period of several weeks to several months as necessary Because of its constricting effect epinephrine hydrochloride 0 25 to 1 0 cc of 1 1000 solution subcutaneously should be on hand for untoward reactions Often more promptly effective is the intravenous administration of histamine in the hospital, with the patient under mild sedation The intravenous method consists *in the daily administration of 2 75 mg per cc of histamine in 250 cc* physiological saline solution over 6 to 8 hours for 10 to 14 days The intravenous procedure builds up a quicker response in the patient than the subcutaneous method but its lasting effects are less so it should usually be followed by maintenance doses of subcutaneous histamine 0 275 mg per cc 1 0 cc 2 or 3 times a week The antihistaminic drugs are usually of no benefit in the treatment of histamine cephalgia

Post concussion Migraine

Sometimes after a trauma to the head the extracranial vessels in the region of the head injury will develop an instability with frequent even continuous dilatation and headache resulting In addition there is fre*quently tenderness and soreness of the scalp in the distribution of the* involved vessel The preferred treatment is double division and ligation of the involved vessel supra orbital temporal or occipital as discussed under surgical treatment farther on The nitroglycerine test as outlined

patient's way of life, it is wisest to allow the patient to make his own decisions rather than to make them for him Further, experience has shown that it is better to have the patient adjust himself to his environment rather than try to change the environment If the problem becomes more complex formal psychiatric treatment may be necessary

Premenstrual-tension Headaches

These are extremely common, a concomitant of premenstrual tension, and are thought to be due to hormonal changes resulting in hydremia and vascular dilatation Such patients usually give a history of bloating, edema of the face or hands, and gain in weight It is quite common, in questioning the patient with migraine headaches to find that whatever other relationships might exist, the patient also tends to have headaches just before or during the early days of menstruation Further, the patient may have observed the passage of copious quantities of urine as the headache subsides The treatment for premenstrual headaches consists of strict limitation of salt beginning one week before the anticipated period and the administration of ammonium chloride 1 0 gm , 4 times a day for 4 to 7 days before the expected onset of menses and continuing through the period of symptoms Sometimes an additional diuretic as described under Cardiac Failure, pages 718 21, may be helpful Hormonal treatment, such as estrogens or progesterone, has not been too satisfactory but may be tried

Histamine Cephalgia

Not much is clearly understood about so-called histamine cephalgia other than that it is a vascular headache, possibly involving predominately the internal carotid artery and its branches The clinical picture that has been described—one of sudden onset, short duration, frequent recurrence nocturnal occurrence, with facial flush and lachrymation which forces the patient out of bed—is uncommon and occurs in less than 10 per cent of our series of vascular headaches

The treatment that has been recommended is desensitization using histamine It is not always successful It may be carried out in the ambulatory patient or in the hospital by the subcutaneous administration of histamine, in graduated increasing doses, according to the new method

10 HILSINGER, R L Headache and Autonomic Imbalance *Laryngoscope*, 1951 LXI p 296
11 BERCEL N A Treatment of Migraine Results with Dihydroergocornine Methane Sulfonate (DHO 180) and Other Ergot Derivatives *Calif Med*, 1950 LXXII p 234

on preceding pages, is useful in establishing the vascular character of the headache and perivascular infiltration with 1 to 2 per cent novocaine (Procaine) hydrochloride will often assure one of the results to be obtained by surgical ligation

Surgery in the Treatment of Vascular Headaches

When a migraine or other form of vascular headache has not responded well to the usual medical means as already outlined, or is intensely severe or becomes intractable, and is *more or less localized or circumscribed*, a surgical approach can be very helpful This consists in ligation of extracranial blood vessels with their associated nerves. Surgical ligation is most useful in localized headaches from involvement of supra orbital, temporal, post-auricular, or occipital arteries In an occasional instance, where a unilateral headache from extracranial vessel involvement is constant and severe, recourse may be had to double ligation and division of the external carotid artery, performed above the superior thyroid artery to prevent retrograde thrombosis from obstructing the adjacent internal carotid artery

BIBLIOGRAPHY

1 WOLFF H G *Headache and Other Head Pains*, Oxford University Press 1948
2 SCHNITKER M T and SCHNITKER, M A "A Clinical Test for Migraine *Jour Amer Med Assoc*, 1947 cxxxv p 89
3 PETERS G A HOLLENHORST R W and GIFFIN M E. Symposium on Migraine Proc Staff Meet Mayo Clinic 1953 xxviii, p 673
4 TUNIS M M and WOLFF H G The Treatment of Headaches' *Med Clin No Amer*, July 1953, p 1251
5 SUSSELMAN S FELDMAN F and BARRERA, S E. Intravenous Injection of Sodium Amytal as a Test for Latent Anxiety, *Arch Neurol and Psych*, 1946 lvi p 567
6 PICKERING, G W Observations on the Mechanism of Headache Produced by Histamine, *Clinical Science*, 1933, 1 p 77
7 HORTON B T The Use of Histamine in the Treatment of Specific Types of Headaches *Jour Amer Med Assoc*, 1941, cxvi p 377
8 SCHNITKER M T Personal communication
9 FRIEDMAN A P Treatment of Migraine *N E J Med*, 1954 ccl, p 600

CHAPTER LXXVII

DISEASES INVOLVING MULTIPLE STRUCTURES OF THE NERVOUS SYSTEM

DISEASES OF AFFERENT OR SENSORY NERVOUS SYSTEM

Tabes, Paresis, and Taboparesis These are caused by syphilis, and their treatment is described in the section on Syphilis

DISEASES OF EFFERENT OR MOTOR NERVOUS SYSTEM

Progressive (Central) Muscular Atrophy Amytrophic Spastic Form. Bulbar Paralysis Glossolabiolaryngeal Paralysis Spastic Paralysis of Adults, Primary Lateral Sclerosis Secondary Spastic Paralysis All of these are progressive conditions, for which very little can be done beyond giving good nursing care guarding against intercurrent infections and injuries and applying symptomatic remedies as remediable symptoms appear Rarely some form of nerve or cord surgery or some orthopedic correction may be indicated For some patients there is the possibility of training muscles whose activity has been lessened by the disease process

Syphilitic Spinal Paralysis Treatment described under Syphilis should be utilized at once Some of these patients will be greatly benefited by it

In this group come the *demyelinating diseases* and *scleroses*, including such subheadings as *Spontaneous Acute Disseminated Encephalomyelitis, Acute Disseminated Encephalomyelitis after Acute Infectious Diseases, Acute Disseminated Myelitis with Optic Neuritis, Multiple Insular or Disseminated Sclerosis and Demyelination, and Diffuse Sclerosis and Demyelination* With the focal lesions of varying size and distribution characteristic of these conditions there is the possibility of a great number of variations in focality of symptoms which lends itself to a complex terminology with many synonyms and the frequent attachment to

diet so that a true deficiency is prevented Other useless agents include vitamin E Cytochrome C trypan red and vaccines

Symptomatic help in spastic cases is given to a limited extent by neostigmine (Prostigmine) when given intramuscularly in a dose of 0 5 mg, gradually increased until a daily intramuscular dose of 2 to 3 mg is given The dose of neostigmine (Prostigmine) bromide by mouth may be slowly increased until a dose of 15 to 30 mg 3 times a day is given This drug does give some relaxation and perhaps facilitates voluntary action but for the most part results have not been very satisfactory

Curare as d tubocurarine is also advocated by some to relax spasm but the serious toxic effects that can result from inadequate control the difficulty of dosage control and the limited usefulness of the drug all have led to very little use of it If it is used one skilled in its use and familiar with its action should initiate therapy

Mephenesin (Tolserol) in 3 to 10 gm doses by mouth daily has also been advocated and may be beneficial in some patients Its action is uneven and does not last very long and unfortunately the drug is helpful only in a limited number of cases

Other agents of value in symptomatic management are urecholine for the depressed bladder function methenamine mandelate (Mandelamine) 3 to 4 gm daily and antibiotics as indicated to control or prevent urinary tract infection Amphetamine (Benzedrine) sulfate or dextro amphetamine (Dexedrine) sulfate by mouth daily is useful in controlling emotional disorders

If pain becomes a problem surgical procedures against pain pathways are more desirable than drug therapy for long continued management

BIBLIOGRAPHY

Diseases Involving Multiple Structures of the Nervous System

1 Association for Research in Nervous and Mental Diseases *Multiple Sclerosis and the Demyelinating Diseases* Williams and Wilkins Co Baltimore 1950
2 PUTNAM T J CHIAVACCI L V HOFF H., and WEITZEN H G Results of Treatment of Multiple Sclerosis with Dicoumarin *Arch Neurol and Psychiat* 1947 LVII p 1
3 SCHUMACHER G A Multiple Sclerosis *Jour Amer Med Assoc* 1950 CXLIII p 1146 Treatment of Multiple Sclerosis *Jour Amer Med Assoc* 1950 CXLIII p 1241

hot packs employed in the treatment of poliomyelitis Joint function should be watched carefully and as soon as pain and spasm permit passive exercises of all joints of involved limbs should be given 3 times a day

Pain is frequently a serious problem and its control gives the patient much needed relief Acetylsalicylic acid 0 6 gm 2 or 3 times a day is helpful but frequently is not potent enough to give complete relief Codeine phosphate, 30 to 60 mg by mouth 2 or 3 times a day is more effective Meperidine (Demerol) hydrochloride 50 to 100 mg intra muscularly, is effective and gives excellent analgesia If pain is exceed ingly severe morphine sulfate 15 mg subcutaneously and repeated 2 or 3 times a day may be necessary Care must be exercised to avoid addiction and if liver damage is present morphine must be given in reduced dosage and in some cases withheld entirely Antispasmodics such as mephenesin (Tolserol) 2 to 5 gm by mouth daily or hot fomentation as recommended in the Kenny method for the treatment of spasm and pain in poliomyelitis frequently give relief

Infections if present should be cleared promptly The diet should be high in minerals proteins and vitamins It is advisable to supplement the diet with added vitamins B_1 and C Thiamine hydrochloride 20 mg 4 times a day and ascorbic acid 25 mg 4 times a day both taken orally are recommended If severe vitamin deficiency exists the patient should receive multiple vitamin therapy as recommended for the vitamin deficiencies

Neuritis whether idiopathic in origin or following the use of preparations of arsenic gold or mercury is often markedly alleviated by the use of dimercaprol (BAL in oil) as described in the treatment of Arsenic Poisoning

Neuritis accompanying diabetes mellitus should be treated as described under that heading

These patients must be observed carefully since paralysis may spread rapidly to other nerves including those of respiration and death from respiratory failure may occur unless prompt use is made of the respirator

Physiotherapy is important in the management of the subsiding acute phase and in convalescence The heat cradle and infra red lamp give relief during the acute phase and as tenderness subsides daily diathermy treatments are helpful Gentle massage with methyl salicylate gradually increased as the patient s condition warrants is most beneficial

Passive exercises are essential to prevent fixation of joints and one full movement of each involved joint should be carried out at least 3 times

the clinical picture of the name of some one who has described a particular symptom complex, such as *Schilder's, Balo's, Pelizaeus Merzbacher's, Scholz's Krabbe's* or *Devic's* diseases

For these diseases there are no specific remedies and, beyond treating the previous infectious disease, if such has occurred, treatment can be only symptomatic as promptly and thoroughly as possible by the measures described elsewhere in this book. Adequate nutrition and high vitamin intake are helpful and residence in a warm climate to avoid chilling is recommended. Patients in whom the condition has become chronic need morale building, avoidance of emotional strain and pregnancy, graded exercises that do not fatigue, physical therapy including massage, active and passive exercise, and muscular re education, if there is inco-ordination and muscle atrophy. In patients with ophthalmoscopic evidence of optic neuritis, repeated lumbar puncture is recommended.

In some of these patients progression may be slow and remarkable remissions do occur, especially in multiple sclerosis. Unfortunately, there is no available therapy capable of producing remissions. The vasodilator drug histamine by either injection or iontophoresis, probably does not accomplish much. Amyl nitrite by inhalation and papaverine hydrochloride, 30 to 60 mg intravenously, are of some value and do improve vision by clearing scotomas in a good per cent of patients. Long term therapy with these agents is unsatisfactory and no lasting improvement has been observed. Other vasodilator drugs such as aminophylline, belladonna, alcohol as whiskey or wine, and antihistaminic drugs are also without any real value in management.

Sympatholytic and adrenolytic compounds, such as tetra ethyl ammonium (Etamon) chloride, 0 5 to 1 2 gm doses intramuscularly 3 to 6 times a week, benzazoline (Priscoline) hydrochloride, 25 to 50 mg 3 times a day and nicotinic acid (Niacin), 50 to 100 mg daily, may all show temporary helpful action, but do not prove of value in long term treatment.

Anticoagulant therapy with bishydroxycoumarin (Dicumarol) has shown some promise but the difficulty in maintaining adequate prothrombin levels and the fact that the disease does recur during therapy have limited its usefulness. If anticoagulant therapy is given, it should be carried out as described under Myocardial Infarction.

Ephedrine, caffeine, adrenocortical extract and desoxycorticosterone, although at one time enthusiastically recommended, are of no value in management. Vitamins of the B complex including B_{12}, have no useful role other than that they must be given in adequate quantities in the

mine as recommended in neuritis is helpful Physiotherapy is most useful and after the acute stage of the disease has subsided this treatment has much to offer The measures recommended for neuritis are also effective in this condition

Neuromata

Tumors located on nerve structures may consist of nerve tissue or fibrous tissue and may occur singly or in large numbers in widely distributed areas Depending on the type location and distribution various entities such as plexiform neuroma generalized neurofibromatosis (von Recklinghausen s disease) tubercula dolorosa and amputation neuromata are described

Treatment should be surgical removal when, through growth or location of the tumor mechanical interference with function is brought about Since there is a tendency for these tumors to become malignant it is wise to have them removed if they are not too numerous and if other conditions make surgery practical

Diseases of the Cerebral Nerves

Of the many affections of cerebral nerves that occur whether primarily or secondary to disease elsewhere the most commonly encountered are toxic amblyopia true trigeminal neuralgia Bell s palsy Meniere s syndrome and torticollis

Toxic Amblyopia

Amblyopia should be watched closely by an ophthamologist who through careful visual field measurements can follow its course

Dimness of vision is commonly caused by a toxic effect of arsenic ethyl and methyl alcohol lead quinine or tobacco on the retina or optic nerve Lack of vitamin A may also lead to impaired vision

Treatment should consist of a careful search for the causative factor and its elimination If arsenic is producing the lesion the use of dimercaprol (BAL in oil) as described for Arsenic Poisoning is advised

Vitamin A deficiency is to be treated as recommended under Vitamin Deficiencies In toxic amblyopia vitamin A 25 000 U S P units daily by mouth should be prescribed as a supplement to a well balanced high vitamin diet

The eyes should be protected from bright lights and rested as much

CHAPTER LXXVIII

DISEASES OF THE PERIPHERAL NERVES

The peripheral nerves may be impaired directly by infection, metabolic disease toxins, trauma, tumors, and vitamin deficiencies or they may be involved by diseases primarily affecting other organs or structures of the body

Neuritis

Treatment of this condition consists of removal or relief from the causative factor and of measures directed toward relief from pain prevention of deformity and the return of function

Acutely ill patients should be in bed and should remain on bed rest until the heart, if it is involved, has become capable of meeting the increased demands placed upon it and until the muscles are strong enough to bear increased activity The heart rate serves as an excellent guide since increased activity will immediately produce a tachycardia if impairment is present The bed clothing should be light and arranged to prevent pressure on sensitive muscles A cradle over the legs is helpful, and when fitted with a source of heat, serves also as an excellent means of supplying heat to the affected limbs A foot board should be prepared in such a way that the feet will be able to rest comfortably against it It should be so placed that the patient may rest on his back and still have support from the board Usually this is accomplished by allowing a space between the foot of the mattress and the board Padding of the board adds to the patient's comfort Patients, who are either too ill to co-operate, or who for some reason are not receiving proper protection against foot drop by a bed board, should have posterior splints applied preferably without bandaging, since the leg must be removed for exercise 3 or 4 times a day Wrist drop requires cock up splints

Every effort must be made from the very beginning to prevent muscle contractures and overstretching Weakened muscles must be protected from overfatigue and spasms relieved by hot fomentation such as the

0 2 gm 3 times a day These failing surgical division of the involved artery is indicated

Bell's Palsy

Paralysis of the facial nerve may result from lesions in the cortex or the muscles, or from involvement of the nerve trunk When the paralysis is caused by a cortical or nuclear lesion the ultimate outlook is much more serious and treatment is usually unsuccessful Cortical lesions producing facial paralysis usually cause hemiplegia or other major paralysis and treatment must be directed toward the over all management with measures for facial paralysis being only a part of the therapeutic procedure (see under Cerebral Hemorrhage)

Facial paralysis produced by a lesion of the nucleus of the facial nerves is uncommon Treatment for this paralysis should be similar to that described in the following paragraphs for the treatment of paralysis resulting from nerve trunk lesions Paralysis of this latter type is common and fortunately it usually responds to therapy

Peripheral facial paralysis or Bell s palsy caused by impairment of the nerve trunk is produced by a variety of causative factors occurs rather commonly and usually responds promptly and excellently to treatment

Therapy should consist of immediate measures to prevent any further nerve damage protection of involved structures, and physiotherapy to accelerate recovery and prevent occurrence of permanent damage

Prompt assessment of the degree of nerve damage by the electrical response of the involved tissues gives valuable information In general Erb s rules serve as an excellent guide to prognosis and extent of therapy required These rules state that if there is no change of nerve or muscle to faradic or galvanic currents the prognosis is good and recovery will take place within 14 to 20 days If faradic or galvanic stimulation show lessened nerve excitability and the muscle excitability is increased to the galvanic current the prognosis is still good and recovery will usually take place in from 4 to 10 weeks When the reaction of degeneration is present recovery is usually long delayed and may be incomplete or fail to occur

Otitis media or any other infection should be cleared promptly by appropriate antibiotic therapy and drainage when indicated If syphilis is present it must be effectively controlled by therapy Diseases toxins and other factors capable of producing nerve damage should be treated as described under Peripheral Neuritis

a day in the early phases Passive exercises should be given for a period of 10 minute 3 times daily as soon as tenderness leaves and this should be continued until the joint can be moved actively through its entire range of motion The interrupted current is useful also at this stage Neostigmine (Prostigmine) bromide 15 mg 3 times a day by mouth, strengthens the neuromuscular action and should be given a trial during this phase of the disease

As soon as muscle action begins to return, an experienced physiotherapist should instruct the patient in muscle retraining With patience and careful supervision excellent function can frequently be secured Active motion should be encouraged but fatigue must be avoided Careful observation of the heart rate will help in preventing undesirable strain

INFECTIOUS NEURONITIS INFECTIVE POLYNEURITIS GUILLAIN BARRE SYNDROME

The etiology of this disease is still obscure and consequently treatment is mainly symptomatic It is important that a correct diagnosis be made in view of the possibility of confusion with post diphtheritic paralysis, poliomyelitis, and other neurotrophic diseases that carry a much more serious prognosis Since this syndrome has many of the aspects of a virus infection, aureomycin, chloramphenicol or terramycin in full therapeutic dosage should be given a thorough trial Dimercaprol (BAL in oil) as recommended for arsenic poisoning should be given During the acute phase patients must be observed closely and, if involvement of the respiratory nerves occurs, placed immediately in a respirator to prevent death from respiratory paralysis

Skilful nursing care is essential, and every effort must be made to prevent the development of bed sores The measures outlined for their prevention in patients with hemorrhage or trauma to the spinal cord are recommended

Nutrition must be maintained at a high level A diet rich in proteins, minerals and vitamins prepared in accordance with the patient's preferences should be supplied Supplemental thiamine hydrochloride 20 to 30 mg by mouth 3 times a day, folic acid 10 mg by mouth times a day, and Vitamin B_{12} 15 micrograms given parenterally 2 or 3 times a week are recommended

Contractures spasm overstretching of muscles and joint fixation and deformity must be relieved or prevented whenever possible Neostig

Meniere's Syndrome

Treatment for this symptom complex varies with the cause and the response of the individual to the various measures available. Attacks produced by acute or chronic infections usually clear when the infectious process is controlled. If the patient is taking such toxic agents as alcohol, arsenic, nicotine, quinine, and salicylates, their use should be eliminated. Hemorrhages secondary to various blood dyscrasias may be causative and when the underlying condition is corrected the vertigo disappears. Brain tumors, degenerative central nervous system diseases and circulatory diseases causing pressure on or alteration of the normal dynamics of the labyrinth should be removed or corrected when possible. Many cases exhibit no detectable etiological factor but fortunately respond to therapy directed toward dehydration of the labyrinth, increasing its blood supply, or depressing the vagus nerve response to increased labyrinth activity.

Vertigo attacks are frequently abolished or considerably reduced in severity by a low salt diet as described on page 746, when continued for many months. The effectiveness of the low salt diet regime is further enhanced by potassium chloride, 4 to 6 gm. daily. This salt may be given as a 25 per cent solution (1 teaspoonful containing 1 gm.) in fruit juice, preferably after meals. Care must be taken, if there is any renal impairment, to avoid potassium intoxication. In general, the potassium should not be continued longer than or 3 weeks. At that time ammonium chloride may be substituted for the potassium chloride with good effect. This should be continued in 6 to 10 gm. doses daily for 4 days a week for 2 or 3 weeks and then gradually discontinued to be followed by another course of potassium chloride if the vertigo still persists.

Patients failing to respond to the low salt dehydration regimen should be given a trial on nicotinic acid (Niacin), 50 to 100 mg. by mouth 3 to 6 times a day. Occasionally severe cases will require 100 mg. intravenously for satisfactory relief. Patients receiving this drug must be warned about the flushing and unpleasant reactions that can occur following its use.

If a satisfactory response is not secured by the preceding measures, diphenhydramine (Benadryl) hydrochloride, 50 mg. by mouth 3 times a day, or dimenhydrinate (Dramamine), 50 to 100 mg. by mouth 3 times a day, occasionally gives excellent results.

A small group of these patients show sensitivity to histamine and are relieved when they are desensitized. Histamine sensitivity is determined

as possible, and all strain should be avoided All possible contact with the offending toxin must be prevented

True Trigeminal Neuralgia Tic Douloureux

Treatment for this painful and at times very serious affection may be very difficult If attacks are at frequent intervals, meperidine (Demerol) hydrochloride, 100 mg orally 2 or 3 times a day, used temporarily, will give considerable relief Care must be exercised to avoid addiction and, if attacks occur at frequent intervals over long periods of time, narcotics should not be used

Neuralgic pains originating from the sphenopalatine ganglion can usually be relieved promptly by cocainization of the ganglion within the nasal cavity

Trichlorethylene (Trethylene) inhalation frequently gives considerable relief from the pain A dose of 20 to 25 drops is sprinkled on gauze, the patient assumes a supine position with the gauze placed over the nose and inhales through the gauze as long as the odor of trichlorethylene is detectable The procedure may be repeated 3 or 4 times a day for a month if necessary Occasional spraying of the side of the face with ethyl chloride will give relief Thiamine hydrochloride given parenterally in a dose of 50 to 100 mg daily has proved helpful and may be tried Vitamin B_{12} 1000 micrograms daily, is useful

All sources of irritation, infections, nervous tension, or physical stress and strain should be removed Diathermy often gives gratifying results

Neuralgias that do not respond favorably to the measures above should be treated surgically The surgical treatment giving the best results is section of the fifth nerve intracranially in the posterior fossa

Alcohol injections, although recommended by some physicians, can be dangerous, and the results are not as satisfactory as surgery

Trigeminal Pain of Vascular Origin

Facial pain in this region is often of vascular origin and should be distinguished from true trigeminal neuralgia or tic douloureux This can be done by placing a 0 4 to 0 6 mg tablet of nitroglycerine under the tongue If the pain is of vascular origin it will be relieved by this and then it should be treated with vasodilators such as benzazoline (Priscoline) hydrochloride 25 to 50 mg 4 times a day, nicotinic acid (Niacin), 50 to 100 mg a day, sublingual nitroglycerine, 0 4 to 0 6 mg given as for attacks of angina pectoris, or dioxylline (Paveril) phosphate

fascia must be excised After surgical removal of the contracting structures, overcorrection of the position of the head should be instituted for approximately 6 weeks followed by manipulation and voluntary exercises until normal function is established Unfortunately in some patients such operations may not give satisfactory cure

Spasmodic torticollis frequently presents a difficult problem in therapy Since many cases seem to be psychogenic in origin psychotherapy is important in its management If the patient brings about neck strain or trauma to the neck muscle by virtue of his occupation recreation or other activities this factor should be corrected Corrective relaxing exercises of the neck muscles should be taught and the patient urged to practice them each day

Mephenesin (Tolserol) 2 to 5 gm daily by mouth may afford muscle relaxation and give some relief Mild sedation with chloral hydrate 0 5 gm by mouth 3 times a day or phenobarbital 15 mg orally 4 times a day is helpful especially in the tense type of individual who is unable to relax These patients need considerable rest and relaxation, and any infections local lesions or sources of trauma should be corrected

When conservative measures are not effective the abnormality should be corrected by surgery Usually stretching section or excision of the accessory nerve plus division of the involved muscle is necessary Occasionally it is necessary to divide all nerves serving the muscles attached to the base of the skull Again results are often not satisfactory

Aquired torticollis may result from various causes including bone lesions of the cervical spine habit spasm hysteria eye lesions local muscular inflammation trauma and many others The corrective measures chosen for treatment must depend on the causative factor A common form of acquired torticollis is that resulting from myositis of the cervical muscles This may follow exposure unusual muscle strain arthritis of the neck, and various conditions leading to muscle trauma or inflammation This form of torticollis responds to salicylate therapy heat and gentle massage Usually a hot pack or electric pad applied 2 or 3 times a day for 30 minutes an infra red lamp or baking given for a few minutes 3 to 4 times a day will provide considerable relief Acetylsalicylic acid 0 3 to 0 6 gm 2 or 3 times a day will relieve the usual case Most severe cases may require heat and meperidine (Demerol) hydrochloride 50 to 100 mg 2 or 3 times a day by mouth for relief Gentle massage and protection from trauma or strain should complete the treatment Recurrent attacks are common especially in

If pain and stiffness are present, the application of warm to hot packs to the painful area, repeated as often and for as long a period as needed, will be helpful. Acetylsalicylic acid 0.3 to 0.6 gm., repeated in 3 to 4 hours, is effective in relieving pain. In cases of severe pain, meperidine (Demerol) hydrochloride, 50 to 100 mg. by mouth or intramuscularly, is recommended.

The paralyzed face should be protected from all injury such as from wind, dust, and cold. A patch worn over the eye on the involved side for protection of the cornea and lavage of the eye with a 2 per cent boric acid solution 2 or 3 times a day are advised. If infection appears, prompt control with appropriate antibiotic therapy is essential. The use of adhesive tape or scotch tape to support the sagging face is desirable.

Infra-red therapy over the face in the parotid region is helpful while nerve tenderness is present. Care must be taken to protect the eyes during this therapy.

As soon as tenderness leaves, the involved facial muscles should be massaged gently 3 times a day for periods of at least 5 minutes. The thumb should be inside the cheek and gentle upward strokes made by the fingers on the outside.

Neostigmine (Prostigmine) bromide, 15 mg. 3 times a day, strengthens the nerve impulses and should be given during the paralysis. Thiamine hydrochloride, given in 100 mg. doses intramuscularly daily for 4 weeks and then 3 times a week until recovery, is thought by some to be helpful in promoting recovery. It is definitely of value if there is any evidence of thiamine deficiency, but in the absence of this deficiency it is doubtful whether the drug will have any value. Cortisone, 100 mg. every 6 hours for the first 3 or 4 days, may be helpful. As recovery occurs, this dose should be reduced to 50 to 100 mg. daily and stopped after 10 to 14 days.

As soon as the tenderness has disappeared, galvanic current stimulation for about 10 minutes at a time applied 3 times a week to the involved muscles, is helpful in maintaining muscle tone and nutrition and promoting earlier recovery. It should be stopped when voluntary muscle contractions appear between treatments.

If recovery has not occurred in from 4 to 6 months the patient should be seen by a neurosurgeon, and the possibility of nerve anastomosis should be considered. The most satisfactory surgical procedure is the anastomosis of the central end of the hypoglossal nerve to the distal end of the facial nerve. Surgical consultation and surgery should not be delayed too long if best results are to be secured.

use of 20 to 30 cc of 0 5 per cent procaine hydrochloride solution injected around the nerve just as it goes behind the clavicle under the sternocleidomastoid muscle will be satisfactory This may control the condition If blocking fails or gives only temporary relief crushing of the nerve or phrenicectomy will be necessary Great care must be taken to sever any accessory branches of the phrenic nerve Intractable cases are generally of psychosomatic origin and require psychotherapy

Scalenus Syndrome Cervical Rib

Pain numbness cyanosis and weakness of the arm or hand can be caused by stretching and pressure on the roots of the nerves to the arm where they pass over the first or a cervical rib in the narrow angle made by the attachment of the anterior scalenus tendon Generally this condition is seen in young women and in the individual whose occupation keeps the arm down at the side or drags down the shoulder Treatment should consist of measures to relax any scalenus spasm—heat gentle massage rest of the muscle and support of the extremity Occasionally simple measures are sufficient such as the use of 3 small pillows, 2 placed diagonally to form an inverted V the third horizontally across the apex of the V to form a trough for the shoulders but usually further difficulty occurs and it becomes advisable to treat the condition surgically Good results are usually secured by division of the scalenus tendon at the point where it attaches to the first or cervical rib or to the cervical rib s fibrous extension This permits the subclavian artery and the nerve roots to slide down and forward and thus free themselves from pressure and tension Relief should be apparent almost immediately

Sciatica

A painful low back may result from many causes the most common being *arthritis fibromyositis herniation of* the nucleus pulposus in one or more places tense fascia lata and congenital lesions of the lower spine To be effective treatment must be preceded by a careful diagnostic evaluation so that proper therapeutic measures may be directed toward relieving the underlying disease Patients with sciatica caused by arthritis *or fibromyositis* should receive the treatment advised elsewhere for these diseases plus the following measures directed toward relief of the sciatica Sciatic pain caused by herniated nucleus pulposus

by the intradermal injection of 0 50 cc of a 1 10,000 solution of histamine acid phosphate into the skin of the flexor surface of the forearm A positive test is present, if there appears within 5 minutes a bleb over half an inch in diameter exhibiting pseudopods of 1 inch or more and an area of erythema 2 or 3 inches in diameter Desensitization varies with the individual but usually good results are secured when histamine acid phosphate 1 10,000, has been given subcutaneously in an initial dose of 0 05 cc for 3 days and then the dose is increased to 0 1 cc If no reaction occurs, the dose after 2 days should be increased to 0 2 cc and 2 days later, in the absence of reaction, further increased to 0 3 cc, and so on until a dose of 1 0 cc is well tolerated The dilution is then to be changed to 1 1000 and an initial dose of 0 12 cc given for 2 days In the absence of reaction this dose is to be increased by 0 02 cc every second day until 1 0 cc of this dilution is well tolerated The drug should then be given in that dose 2 times a week until symptoms remain in abeyance If a reaction occurs, the dosage should be repeated the next day, unless the reaction is severe in which case a 50 per cent reduction in dose should be made, followed by a gradual increase and return to schedule

Tense emotionally unstable patients are aided by small doses of phenobarbital 15 mg 3 or 4 times a day, continued until the attacks are controlled by more specific measures Psychotherapy is beneficial, and frequently proves most helpful

Patients with severe crippling attacks not controlled by the measures above should be seen by a neurosurgeon and surgical section of the eighth nerve recommended Usually section of the vestibular division of the eighth cranial nerve will give prompt and permanent relief

Torticollis Wryneck

Torticollis although usually easily recognized, may present a difficult problem in therapy Congenital torticollis should be recognized early and corrective treatment begun promptly When congenital torticollis is recognized early in infancy and there is no osseus deformity, fibrosis, or other apparent defect of the sternocleidomastoid muscle, passive exercises consisting of overcorrection should be given several times daily It these do not help the condition the deformity should be corrected by surgery without delay This usually consists of dividing the sternocleidomastoid muscle and other contracted fibrous tissue preventing normal rotation of the head Occasionally considerable deep cervical

lumbosacral belt will be helpful and may also be used to give additional support to the back as the patient returns to normal activities

Corrective exercises of relaxed abdominal muscles will be useful and can be easily carried out by having the patient raise his head from the pillow 15 or 20 times each morning before rising Postural corrective exercises are advisable whenever muscular weakness exists Shoes are important and a well fitted shoe with a wide heel of medium height is recommended Obesity is harmful and when present should be treated as described elsewhere Emotional tension abnormal occupational postures, chronic infections and other precipitating factors should be eliminated or corrected whenever possible

BIBLIOGRAPHY

Diseases of the Peripheral Nerves

1 BRAM W R *Diseases of the Nervous System* Oxford Medical Publications 4th edition 1951
2 CANE, E. F Pain in the Neck and Upper Extremity *Med Clinic No Amer* September 1950 p 1333
3 KOVAC R Physical Medicine in Neuromuscular Affections *Med Clinic No Amer*, May 1948 p 779
4 NIELSEN J M *A Textbook of Clinical Neurology* Paul B Hoeber Inc 3rd edition 1951
5 PICKERILL H S and PICKERILL C M Early Treatment of Bells Palsy *Brit Med J* 1945 ii p 457
6 WILLIAMS H L The Present Status of the Diagnosis and Treatment of Endolymphatic Hydrops (Meniere s Disease) *Ann Otol Rhin and Laryng*, 1947 cvi p 614

cases with an underlying cause such as arthritis Traction applied in various ways with the patient in bed is often very helpful. With torti collis a Thomas collar is often advisable

Hiccough Singultus

The host of procedures recommended for the treatment of this condi tion attests to the inadequacy of the available agents in severe persistent cases

Since hiccough is only the manifestation of an underlying disease, either functional or organic, a determined search should be made to dis cover the etiology It is known that hiccough may follow infections, irritations, malignant degenerations, toxic processes, and diseased con ditions anywhere in the body Sometimes it is a manifestation of a virus disease Correction of any abnormal function should be carried out whenever possible If none of these factors exists, the cause may be psychogenic, a case of hiccough that occurs in the absence of organic disease and that does not respond to the usual corrective measures should be treated by psychotherapy

Ordinarily hiccough responds readily to many simple measures. Holding the breath, swallowing water slowly, eating bread or cracked ice rebreathing from a paper bag, or pulling out the tongue and holding it for a short time are all old and effective measures in mild cases

More severe hiccough may require carbon dioxide, 5 per cent, and oxygen, 95 per cent Occasionally a whiff of amyl nitrite will relieve these cases Morphine sulfate, 15 mg subcutaneously or meperidine (Demerol) hydrochloride, 50 to 100 mg intramuscularly, is also effec tive If the hiccough continues, the stomach should be aspirated, and aluminum hydroxide and magnesium trisilicate (Gelusil), 15 to 30 cc, should be given

Muscular antispasmodic drugs have been tried with varying success Quinidine sulfate 0 6 gm intramuscularly, repeated in hourly doses for 2 or 3 hours and then given in oral doses of 0 3 gm every 2 or 3 hours after the paroxysms have ceased, is worth trying Mephenesin (Tol serol) given as described for patients with tetanus, is also useful Scopolamine hydrobromide sublingually 0 3 mg, may be tried

Persistent hiccough is a difficult problem and at times exhausts the resources of the physician In these cases careful search for and correc tion of any possible underlying disease must be made If the condition still persists the phrenic nerve should be blocked In this procedure the

Massage and exercises are of some value in maintaining function of the remaining muscles and orthopedic measures are sometimes indicated to prevent deformities and contractures or to correct them when they have occurred On the basis that phosphocreatin content of muscles is important in muscle contraction some have claimed benefit in the mus cular dystrophies from the daily oral administration of amino acetic acid (Glycin) in doses of 10 0 gm 3 times a day It may be tried but the results from it have not been encouraging Epinephrine and pilocar pine hypodermically have been used to stimulate the autonomic inner vation of the muscles and thereby improve their tone The method of treatment is by the injection subcutaneously of 0 to 0 3 cc of 1 1000 epinephrine and 0 1 to 0 2 cc of 1 per cent solution of pilocarpine hydrochloride daily or every other day up to 60 doses without inter ruption Occasionally this has been of benefit Cortisone and corti cotropin are of no value in the treatment of progressive muscular dystrophy

Werdnig Hoffman Muscular Atrophy

This condition is characterized by progressive degeneration of the motor cells of the spinal gray matter and clinically by muscular atrophy and paralysis The term Werdnig Hoffman is used to designate cases occurring in infancy but other forms occur later in childhood

In this fairly rapidly progressive and fatal affliction there is no known effective treatment Cortisone and corticotropin are of no value Pre vention of infection is important and general hygienic measures of a *supportive nature should be carried out Proper exercises and massage* are useful Orthopedic measures may be necessary to correct deformi- ties The life span is usually brief

Progressive Muscular Atrophy

Progressive muscular atrophy is a slowly progressing degenerative *process of the anterior horn* cells of the spinal cord with resulting muscular paralysis the etiology is unknown Various nosological entities have been defined according to the location of the most prominent atrophy

The most common is the spinal form of Aran Duchenne in which the atrophy begins most often in the small muscles of the hand If the predominant atrophic process involves the bulbar nuclei the condition is named progressive bulbar palsy When in a few instances it involves

responds reasonably well to medical measures, but when these are unsuccessful the herniated disc should be removed by surgery Surgery is indicated if there is functional impairment, or if impairment appears while conservative measures are being followed Similarly congenital defects may require surgery for satisfactory relief from symptoms In general however, much can be gained in many cases by the proper application of the following measures

The spine should receive adequate support during sleep when the muscles are relaxed and there is additional strain on ligaments This can be accomplished by the use of a firm mattress supported by bed boards, so that all sagging of the spine and much of the free movement usual to a sleeping person are eliminated

Muscle spasm is ameliorated by mephenesin (Tolserol), 3 to 5 gm by mouth daily, or tubocurarine chloride may be given, as recommended for tetanus, in the rare severe case

Pain is lessened by acetylsalicylic acid, 0 6 gm every 2 or 3 hours More severe pain requires codeine sulfate, 30 to 60 mg every 3 or 4 hours, in addition to acetylsalicylic acid Meperidine (Demerol) hydrochloride, 50 to 100 mg, or methadone, 5 to 10 mg by mouth or intramuscularly every 3 hours, is also an effective analgesic for sciatic pain

The application of moist hot packs to the tender areas in the lower back relieves spasm and pain Baking with an infra-red lamp and the use of an electric hot pad are also helpful Patients with a tight fascia lata are definitely benefited by exercises directed toward stretching them These exercises should consist of the patient s taking a position with the side of the body toward a wall about 2 or 3 feet away The patient leans against the wall with the extended arm The knees are to be held stiff and the body bent toward the wall at the hips This action will tense and stretch the fascia lata The maneuver is to be repeated on each side 15 to 30 times as ability increases If this exercise is carried out persistently, the fascia will gradually become less tense and the tilting of the pelvis brought about by their tenseness will be relieved together with the associated back pain

Severe muscle spasm and pain originating from a definitely circumscribed area may be relieved temporarily by the injection of 10 to 20 cc of 2 per cent procaine hydrochloride Occasionally excellent results and complete relief follow the breaking of the spasm by procaine infiltration Generally however, the measure gives only temporary relief

Back support in the form of properly fitted corsets, braces, or wide

Massage and exercises are of some value in maintaining function of the remaining muscles and orthopedic measures are sometimes indicated to prevent deformities and contractures or to correct them when they have occurred On the basis that phosphocreatin content of muscles is important in muscle contraction some have claimed benefit in the muscular dystrophies from the daily oral administration of amino-acetic acid (Glycin) in doses of 10 0 gm 3 times a day It may be tried but the results from it have not been encouraging Epinephrine and pilocarpine hypodermically have been used to stimulate the autonomic innervation of the muscles and thereby improve their tone The method of treatment is by the injection subcutaneously of 0 to 0 3 cc of 1 1000 epinephrine and 0 1 to 0 2 cc of 1 per cent solution of pilocarpine hydrochloride daily or every other day up to 60 doses without interruption Occasionally this has been of benefit Cortisone and corticotropin are of no value in the treatment of progressive muscular dystrophy

Werdnig Hoffman Muscular Atrophy

This condition is characterized by progressive degeneration of the motor cells of the spinal gray matter and clinically by muscular atrophy and paralysis The term Werdnig Hoffman is used to designate cases occurring in infancy but other forms occur later in childhood

In this fairly rapidly progressive and fatal affliction there is no known effective treatment Cortisone and corticotropin are of no value Prevention of infection is important and general hygienic measures of a supportive nature should be carried out Proper exercises and massage are useful Orthopedic measures may be necessary to correct deformities The life span is usually brief

Progressive Muscular Atrophy

Progressive muscular atrophy is a slowly progressing degenerative process of the anterior horn cells of the spinal cord with resulting muscular paralysis the etiology is unknown Various nosological entities have been defined according to the location of the most prominent atrophy

The most common is the spinal form of Aran Duchenne in which the atrophy begins most often in the small muscles of the hand If the predominant atrophic process involves the bulbar nuclei the condition is named progressive bulbar palsy When in a few instances it involves

CHAPTER LXXIX

HEREDITARY AND FAMILIAL DISEASES

Some of the more important heredofamilial diseases of the nervous system and muscles are considered in this chapter They are characterized by normalcy at birth which distinguishes them from congenital defects Once the degenerative phenomena have begun, usually in infancy or childhood, they are almost invariably slowly progressive and fatal This group also have been termed the *abiotrophies*

One example of this group of syndromes, Huntington's chorea is discussed on page 936 A few would place multiple or disseminated sclerosis in this group of hereditary and familial diseases This is discussed on page 915 Hepatolenticular degeneration (Wilson's disease) is considered on page 937

Up to the present time there is no specific treatment known for any of them In a few instances of muscular dystrophy and muscular atrophy cortisone and corticotropin have been tried and found wanting For all of them symptomatic measures are the most that can be offered

Muscular Dystrophies Myopathies

The term muscular dystrophy is used to designate certain heredofamilial degenerative diseases of muscles characterized by progressive wasting and paralysis of the skeletal muscles There is no adequate classification of these various disorders but they have been divided into several types depending upon the age of onset, the presence or absence of pseudohypertrophy and the particular groups of muscles first affected On such bases there have emerged (1) the facio-scapulo-humeral type of Landouzy Dejerine (2) the juvenile scapulo humeral type of Erb, (3) the pseudohypertrophic type of Duchenne, and (4) the femoral type of Leyden Moebius

To the present time there is no treatment of value in arresting the progress of the disease In view of the slowly progressing character the general health of the individual should be maintained as well as possible Obesity usually resulting from sedentary habits should be avoided

to maintain activities especially those of a remunerative nature In some orthopedic corrections become advisable

Cerebromacular Degeneration

There are several types of this with involvement of retinae and central nervous system such as Tay Sach s disease or amaurotic family idiocy early juvenile form of Bielschowski later juvenile form of Vogt Spielmeyer and later juvenile form of Kufs

For any of these types there is no known treatment effective in altering the course of the disease In the case of the infantile and juvenile forms of these diseases the parents should be advised that subsequent children will probably suffer from the same affliction Steps should be taken to prevent intercurrent infections in the patient General supportive treatment exercise short of fatigue directed toward increasing co ordination and symptomatic therapy should be carried out

Myoclonic Epilepsy

Myoclonic epilepsy or Unverricht s familial myoclonic epilepsy is a familial condition occurring chiefly in girls with myoclonia generalized epileptic attacks gradual diminution of intelligence and finally organic dementia

The myoclonic twitchings and the convulsions should be controlled as outlined under Epilepsy There is no treatment effective for the progressively downhill course of myoclonic epilepsy An attempt *should be made to maintain good general health*

Epiloia Tuberous Sclerosis

Tuberous sclerosis is a developmental defect of the neuroectodermal system with multiple tumors and is characterized by mental retardation epileptic seizures and adenoma sebaceum like skin lesions The convulsive seizures should be controlled by anticonvulsant measures as outlined under Epilepsy *There is no known effective therapy for the* progressively downhill course of the disease Intracranial tumors because they are multiple should not be removed unless there is evidence of increased intracranial pressure which should then be relieved Tumors elsewhere such as in the kidney may be removed if it seems reasonable to do so Associated congenital anomalies as harelip cleft palate and spina bifida should be repaired as indicated

the peroneal muscles of the lower extremities it is called Charcot Marie Tooth disease Quite commonly the spinal form has associated involvement of the pyramidal tracts in the cord and is then called amyotrophic lateral sclerosis

The disease process usually progresses very slowly so that every effort should be made to maintain optimum health No specific measures are known Braces and supports for the ankle or foot are often helpful, Arthrodesis of the ankle joints in selected cases may be useful

Progressive Interstitial Hypertrophic Neuritis

This affliction, with its palpably enlarged peripheral nerves and ascending atrophy of muscles, sometimes with pain, probably belongs in the same category with Charcot-Marie Tooth disease For it there is no known specific treatment, but general hygienic measures with maintenance of good health should be emphasized Every effort should be made to prevent contractures and deformities

Hereditary Ataxias

The hereditary ataxias include a rather wide variety of clinical disturbances caused by degeneration in the cerebellum or its connections These disturbances have in common symptoms referable to some portion of the cerebellar system that is in the afferent spino-cerebellar olivo cerebellar, or ponto cerebellar connections, in the cerebellar parenchyma, or in the efferent system of the dentate nuclei and superior peduncles Depending upon the predominant localization of the lesions and corresponding symptomatology, a number of disease syndromes have been differentiated some bearing the proper name of their discoverers such as Friedreichs ataxia, Sanger-Brown type, ataxia of Ferguson and Critchley progressive cerebellar degeneration, and hereditary (familial) spastic paraplegia There is no known specific therapy for any of these Usually they are progressive diseases but fortunately progression is often slow Consequently an optimistic attitude is desirable for these patients The patient's nutrition should be maintained by an adequate vitamin rich diet supplemented by vitamin preparations especially the vitamin B complex Massage will be helpful along with warm baths Exercise should be encouraged short of marked fatigue In some patients co-ordination can be improved by co ordinating muscle activities Morale can and should be helped by encouraging the patient

mg , and diphenhydramine (Benadryl) hydrochloride, 50 to 100 mg given 4 times a day, has been shown to be of definite value Some patients do better on cycrimine (Pagitane) hydrochloride either alone or in combination with diphenhydramine The dose of cycrimine must be carefully adjusted to the patient s needs In the elderly arteriosclerotic individual an initial dosage of 1 25 to 2 5 mg 3 or 4 times a day gradually increased to 15 or 20 mg total daily dose as dictated by the patient s response is recommended Care must be taken since these patients may develop untoward effects such as dryness of mouth, blurring of vision epigastric distress dizziness and disorientation In the postencephalitic case 5 mg 2 to 3 times a day initially to a total daily dose of 30 to 40 mg is suggested depending on the patient s need and the degree of toxic effect

Ethopropazine (Parsidol) hydrochloride 50 mg 3 times a day slowly increased to 100 mg 3 or 4 times a day is also effective and gives fewer undesirable side effects than other agents It may be combined with other agents to enhance the effect

Benzotropine (Cogentin) sulfonate combining the properties of atropine with those of the antihistamines is also a useful agent It is given in a dose of 0 5 to 2 mg daily Usually an initial dose of 0 5 mg at bedtime is satisfactory and this is increased to 1 0 mg if needed In some patients the dose must be gradually increased by 0 5 mg increments at weekly intervals in order to secure maximum effect Occasionally 4 to 6 mg a day is needed Usually the patient with the postencephalitic type of Parkinsonism requires larger doses and tolerates the drug better Untoward effects are similar to those seen with atropine and with diphenhydramine (Benadryl) It can be used in combination with other agents which enhance its value

Caramiphen (Panparnit) hydrochloride 12 5 mg 5 times a day increased slowly until 100 to 600 mg are given daily may be used Usually 200 to 400 mg a day is effective

It is apparent from the above that there are many agents for the treatment of Parkinsonism Sometimes one sometimes another proves most effective for the particular patient It is therefore necessary to reevaluate therapy continually, adding another or shifting to a new agent or a combination of agents as conditions indicate

Very active physiotherapy should be combined with drug therapy An organized program of exercises corrective measures and educational procedures is most helpful Finally the psychological aspects must be

CHAPTER LXXX

DISEASES OF THE BASAL GANGLIA AND SUBTHALAMIC NUCLEI

Diseases under various names—Parkinson's disease (paralysis agitans), post encephalitic parkinsonism, progressive atrophy of the globus pallidus arteriosclerotic parkinsonism parkinsonism following poisons, hepatolenticular or progressive lenticular degeneration (Wilson's disease) dystonia musculorum deformans, double athetosis progressive rigidity with athetosis, and chronic hereditary (Huntington's) chorea—have in common an irremediable progression, sometimes slow, sometimes rapid and muscle rigidity with or without tremors, sometimes fine, sometimes coarse causing increased difficulty in walking until the patient becomes bedridden The only treatment that is at all effective is the use of drugs to lessen muscle rigidity and tremors and so to improve locomotion and increase what the patient can do with his hands Until recently tincture of belladonna, 15 drops 3 times a day scopolamine 0.4 to 0.6 mg 4 to 6 times a day or stramonium leaves, 0.2 gm, or tincture of stramonium, 1.0 cc increased slowly to the maintenance dose, were used If given judiciously in dosage short of any toxicity, they were often definitely ameliorative Usually increases in dosage can be made at 3 day intervals until 6 to 8 times the initial dose is reached More recently amphetamine (Benzedrine) sulfate 5 to 10 mg in the morning and 5 to 10 mg at noon added to the hyosine or stramonium has been more satisfactorily effective Diphenhydramine (Benadryl) hydrochloride, 25 to 100 mg 3 or 4 times a day, will also be helpful and is enjoying wide use Still more recently, trihexyphenidyl (Artane) has been used with good effect in these patients, it should be given in gradually increasing amounts by mouth until a dose of 2 mg 2 to 5 times a day is reached and the best results obtained This usually averages 2 mg 5 times a day but more may be required Better results may come from combining it with other drugs, it may be tried in combination with Artane 8 to 10 mg, and phenindramine (Thephorin) tartrate 100 to 200 mg divided into 4 equal doses and given at equal intervals during the day Also a combination of scopolamine hydrobromide 0.3 to 1.2

5 SCHWAB R S and TILLMAN W R Artane in the Treatment of Parkinson s Disease A Report of Its Effectiveness Alone and in Combination with Benadryl and Panparnit, *N E J Med*, 1949 CCXLI p 483
6 SCHEINBERG I H and GITLIN D Deficiency of Ceruloplasmin in Patients with Hepatolenticular Degeneration (Wilson s Disease) *Science*, 1952 CXVI 484

carefully considered Proper psychotherapy at times does more than any of the drugs

As in epilepsy, with most of these drugs in the treatment of Parkinsonism, it is wisest to increase or decrease gradually the dose, when substitutions are introduced the new drug should be increased gradually while the old one is being decreased

Hepatolenticular Degeneration Wilson's Disease

Patients with Wilson's disease should be given a course of dimercaprol (BAL in oil) as recommended for arsenical poisoning This may be repeated 2 or 3 times if results warrant further use Some patients exhibit a promising response to this therapy Apparently there is an abnormality in copper metabolism since high levels of copper are found in the liver and the lenticular nucleus of the brain and there is a high urinary excretion of copper There is also a low level of ceruloplasmin (a blue alpha globulin), which carries copper

Nursing care, teaching the patient occupations within his limitations, mechanical aids to locomotion, protection from falls and other injuries, maintenance of morale in all possible ways including psychotherapy, a nutritious diet with, for many patients, feeding by nurse or a member of the family are all obvious musts in the treatment of the diseases of this group

BIBLIOGRAPHY

Diseases of the Basal Ganglia and Subthalamic Nuclei

1 BERGER F M, and SCHWARTZ R P 'Oral 'Myanesin in Treatment of Spastic and Hyperkinetic Disorders," *Jour Amer Med Assoc*, 1948, cxxxvii, p 772

2 BUDNITZ J 'The Use of Benadryl in Parkinson's Disease A Preliminary Report of 8 Cases' *N E J Med*, 1948, ccxxxviii, p 874

3 EFFRON A. S, and DENKER P G "A Clinical Evaluation of Certain Antihistaminic and Antispasmodic Drugs in Parkinson's disease' *Jour Amer Med Assoc*, 1950, cxliv, p 5

4 SCHWAB R S and LEIGH D "Panparnit in Treatment of Parkinson's Disease,' *Jour Amer Med Assoc*, 1949 cxxxix p 69

PART XXII

DISEASES AFFECTING MULTIPLE SYSTEMS

CHAPTER LXXXI

Allergy

In this section will be considered allergy in its usual sense that is, hay fever asthma hives (dermatologic reactions), serum sickness and drug allergy The treatment of asthma is considered under Diseases of the Bronchi page 564

Hay Fever

Hay fever may be seasonal, in which case it is usually due to a specific etiological factor or perennial in which case the symptoms are essentially those of what is called vasomotor rhinitis with a specific etiology difficult to determine In the case of the former, every attempt should be made to discover the allergen usually an inhalant, and either eliminate it from the environment remove the patient from the source or attempt to desensitize the patient In cases of vasomotor rhinitis, symptomatic therapy is about the most one can offer along with proper prevention and treatment of associated upper respiratory tract infections

The determination of the offending agent or agents—for they may be multiple and are usually inhalants—is the most important first step in the prevention and treatment of nasal allergy The allergens can range from dusts animal emanations to molds fungi and pollens The predominant distribution of varieties of pollens in different localities should be determined locally

Every reasonable attempt should be made to eliminate the offending substances House dusts and other dusts can be minimized by using covered or rubber mattresses and pillows and avoiding rugs draperies and overstuffed chairs in the bedroom Linoleum makes a satisfactory

the constitutional symptoms that go along with hay fever, nor do they help when there is marked nasal edema

Still very effective and sometimes more helpful than the antihistamines is the much older remedy ephedrine, either hydrochloride or sulfate In the usual dosage 24 to 48 mg it may be too stimulating for some patients To counteract this effect there are numerous preparations combining ephedrine with either phenobarbital amobarbital (Amytal) or pentobarbital (Nembutal) usually 15 mg per capsule These are particularly useful preparations for bedtime administration Epinephrine (Adrenalin) hydrochloride on the other hand is seldom necessary in hay fever when the symptoms are confined to the upper respiratory passages When there is marked nasal edema 0 3 to 0 6 cc of 1 1000 solution subcutaneously at intervals is very effective Cortisone and corticotropin (ACTH) usually have no place in the treatment of hay fever

For the more protracted perennial vasomotor rhinitis the avoidance of nasal irritants is very important With mild symptoms no treatment may be necessary During more severe symptoms one of the antihistamines with lesser sedative effects may be used 1 to 3 times daily as necessary or ephedrine sulfate may be given in doses of 24 mg morning and afternoon and combined with a sedative at bedtime Since in many of these cases secondary infection has taken place an antibiotic chosen for sensitivity against the organism may be tried As one is dealing with an allergic individual considerable caution should be exercised in instituting antibiotic therapy It should be determined from the history whether the antibiotic has ever been given to the individual before and whether there was any reaction to it It is better in these cases not to use an antibiotic unless it is necessary and then it should be given by mouth rather than parenterally because of a lesser incidence of reactions from the oral route

Further in the way of symptomatic treatment in hay fever topical applications may be used Generally the otolaryngologists have condemned nasal applications and sprays because of a tendency when used for protracted periods for increased compensatory swelling and congestion to occur when the constricting effects of the drug have worn off this leads the patient to increase the frequency of local applications with the establishment of a vicious cycle With this concept in mind any topical applications should be used sparingly Numerous 1 to 2 per cent ephedrine sulfate solutions and nasal jellies have been available for years and are effective Phenylephrine (Neosynephrine) hydrochloride

sensitivity beginning three months before the expected symptoms with the injections given five to seven days apart Unless one deals extensively with the treatment of allergies it is best not to try to give injections along with the occurrence of pollenation during a hay fever season In the more perennial cases it may be very helpful once the maximum dose and titer has been reached to give an injection of the maximal dose at weekly intervals the year round

A tourniquet and a syringe containing as much as 1 0 cc of 1 1000 epinephrine (Adrenalin) hydrochloride should always be on hand at the time of a desensitization injection in case of a reaction Should a reaction occur with fainting palpitation pallor and so on, a tourniquet should be applied firmly above the site of injection between it and the heart and 0 3 to 0 6 cc of the epinephrine injected immediately sub cutaneously into the other arm Artificial respiration as described on page 372 may be necessary

Serum Reaction

The treatment of acute reactions following the administration of specific immune sera is discussed on page 16

Serum Sickness Urticaria and Angioneurotic Edema

Although serum sickness urticaria and angioneurotic edema are usually grouped together in discussion they seldom occur together in a single individual This is true particularly of urticaria and angioneu rotic edema But their backgrounds are often similar namely allergy

The treatment of angioneurotic edema is discussed on page 776

Serum Sickness

The anaphylactic or immediate reaction following the administra tion of serum or antitoxin should be treated promptly with subcutaneous epinephrine as outlined on pages 15 and 16 under desensitization reac- tions The so-called anaphylactoid reaction also called accelerated serum reaction that occurs 2 to 5 days after the serum administration is simply an earlier manifestation of the usual serum reaction that occurs

floor covering and damp mops should be used for housework. Molds and fungi may be controlled by discouraging mildew and keeping the entire house dry, particularly the basement. The removal of pet cats, dogs, and horses when necessary is usually very successful in alleviating suffering in those found sensitive to such animal danders.

Conversely, removing the individual from the environment is helpful if he can be sent to an area where the pollen to which he is sensitive does not exist, or is present only in small amounts. Mere change of climate may not be sufficient. In the same way, a child should not be sent to a summer camp where his allergic reaction may be made worse.

For the *acute attack* of hay fever or allergic rhinitis, a new chapter in the symptomatic treatment has been added by the introduction of the antihistaminic substances. Although they do not appear to interfere with the antigen-antibody reaction, the antihistaminic substances may displace histamine from the cell receptor and in some way protect the cell so that histamine is not effective upon it.

There are numerous antihistamines available for use, and proper selection depends on the side reactions that may occur. These may consist of drowsiness, headache, dryness of the mouth, constipation, occasionally nausea, vomiting, diarrhea, and sometimes excitation, palpitation and vertigo. Two of the most commonly used antihistamines have been diphenhydramine (Benadryl) hydrochloride and tripelennamine (Pyribenzamine) but both are common offenders in the causation of sleepiness in the usual dosage of 50 mg., 3 or 4 times a day. Sometimes a reduction in dosage to 25 mg. 3 or 4 times daily, or 25 to 50 mg. 1 or 2 times daily, may be sufficient to control symptoms and avoid drowsiness. Other effective antihistaminics that may be tried include chloroprophenpyridamine (Chlor-trimeton) maleate 4 mg. every 4 to 6 hours, pyrilamine (Neo-antergan) maleate and phenindamine (Thephorin) tartrate in 25 mg. doses, orally 2 to 4 times a day. Since phenindamine (Thephorin) tartrate usually stimulates the central nervous system and keeps patients awake, it may be used in a dose of 25 mg. 3 times during the day, with diphenhydramine (Benadryl), 25 to 50 mg., substituted at bedtime to insure sleep. This combination is especially valuable for those patients made too drowsy by antihistamine therapy.

In using the antihistamines it should be remembered that they have multiple pharmacological actions and that they are only palliative, not curative, in the treatment of allergic manifestations, in this case vasomotor rhinitis or hay fever. In their palliative effect they usually control quite well the itching, sneezing, and rhinorrhea. They may not benefit

foci of infection and psychogenic causes the possibilities become in numerable

In acute urticaria local application of calomine lotion with 1 per cent phenol and systemic administration of one of the antihistamines—diphenhydramine (Benadryl) hydrochloride or tripelennamine (Pyri benzamine) hydrochloride 50 to 100 mg 3 or 4 times a day or ephe drine sulfate, 24 mg 3 times a day are often effective In more acute phenomena epinephrine hydrochloride 0 3 to 0 6 cc of a 1 1000 solu tion subcutaneously may be needed The steroid hormones corti cotropin (ACTH) and cortisone, are seldom necessary unless the lesions are very severe

In chronic urticaria symptomatic treatment should be carried out for relief of the patient while the causes are being sought Often it is well to remove the patient from his immediate environment and place him at bed rest in a hospital A psychogenic factor often important should be dealt with very carefully, and all sedative drugs which possibly might have an urticariogenic propensity should be avoided If an ali mentary antigen is suspected or found forcing fluids and the use of saline laxatives are useful Phenolphthalein containing laxatives should be avoided Soothing baths of starch or oatmeal gruel for 20 to 30 minutes several times a day are helpful

The steroid hormones corticotropin (ACTH) and cortisone may be used in chronic urticaria when symptoms are severe and intractable with the understanding that their benefits are usually only temporary Corticotropin may be given subcutaneously 25 mg 2 or 3 times a day or as a longer acting preparation (Acthargel) 40 mg per day as one injection Cortisone may be given by mouth 100 to 200 mg per day in divided doses In chronic urticaria neither drug should be administered longer than for a period of 10 to 14 days They may be used in con junction with the treatment outlined in the paragraph above

Drug Allergy

In the therapy of drug allergy it is useful to keep certain prin ciples in mind It is always well to remember that any rash or any fever in a patient may be caused by some medication the patient is taking Drug allergy is acquired and an interval of at least 5 days usually elapses between first exposure and the appearance of the allergic manifestations The manifestations of a drug reaction will usually begin to disappear if they are not entirely gone 2 to 3 days after the offending substance

in 0 25 per cent solution is useful Phenylpropanolamine (Propadrine) hydrochloride as a 1 per cent aqueous solution may be applied to the nasal mucosa as a spray or instillation, or may be used as 0 66 per cent jelly locally Tripelennamine (Pyribenzamine) hydrochloride is also supplied as a 2 per cent solution for spray or as a 0 5 per cent solution to be instilled as nose drops and may be tried A somewhat stronger and longer lasting preparation, but definitely more irritating, is naphazoline (Privine) hydrochloride as a 0 05 per cent solution applied as drops into each nostril 2 or 3 times a day Unfortunately unless care is taken, this preparation can cause severe damage to mucous membrane

For the conjunctivitis with burning and smarting of the eyes, an ophthalmic suspension of 2 5 or 5 0 per cent cortisone acetate is most effective One or two drops may be placed in the conjunctival sac as often as every hour during the day and every two hours at night Various collyria containing ephedrine may be used similarly

The *definitive treatment* of allergy, particularly of hay fever and asthma, is a long-term one consisting of desensitization when acute symptoms are not present Desensitization consists of injections of increasing strength of solutions of the offending allergen for the purpose of increasing the tolerance of the allergic person to the specific allergen The principles of desensitization with skin testing, are discussed under Bronchial asthma page 564 In general, desensitization by injection should be tried chiefly for inhalants such as pollens, molds, bacteria and house dusts which cannot be readily eliminated or significantly reduced in the environment Desensitization by injection to foods and animal emanations is not often successful, and usually they can be avoided by the allergic individual Desensitization to eggs, wheat, milk or other common foods may be accomplished by gradually increasing amounts by oral ingestion over a period of several months

The injection method of desensitization for pollens dusts, bacteria and molds can never be a fixed schedule because of variations in the individual and in the environment In the case of timothy, ragweed molds, and so on, depending on skin sensitivity tests, a beginning dose may start at 0 05 cc of 1 10 000 dilution Likewise, in the case of house dust, a dose of 0 05 cc of 1 100,000 dilution may be used to begin the series of injections Such injections are usually given subcutaneously in the lateral aspect of the middle portion of the upper arm low enough to allow a tourniquet to be placed around the arm above the site of injection, if necessary, as described further under reactions As stated under bronchial asthma, injections are best given for the strictly seasonal

effects of epinephrine or its analogs Chlorprophenpyridamine (Chlor-trimeton) maleate for injection in a dose of 10 to 20 mg diluted in 10 to 20 cc of saline and given slowly intravenously is also proving very effective Frequently the addition of 5 to 10 mg of this antihistaminic to the drug to be administered will prevent an allergic reaction as, for example, with penicillin injections

In the milder and more prolonged reactions the first step is to stop the administration of the harmful drug In most instances the mani festations will begin to clear up in 1 to 3 days In some cases as in skin reactions from penicillin the manifestations may last for weeks or months Occasionally when several drugs are being administered it may not be known which one is the offender In such circumstances all medications should be stopped except any that are needed to save life or that are known not to cause reactions Occasionally the nature of the reaction itself will give a clue to the cause Appended to this section is a list of drugs taken from Carr that have been reasonably well established as causes of certain allergic reactions in man including bone marrow depression the list may be consulted as a guide

The next step is to promote excretion of the drug This is best accomplished by forcing of fluids by mouth and parenterally if neces sary Amounts of 2500 to 3000 cc to insure a diuresis well over 1500 cc in 24 hours should be used If parenteral adminis ration is used both saline and glucose may be given unless there is reason for sodium restriction

The antihistamines may be helpful in further combatting the allergic manifestations given orally in doses of 50 or 100 mg 3 or 4 times a day It may be generally stated that the antihistamines appear to be often but not invariably useful in urticaria and angioneurotic edema often but not invariably disappointing in contact dermatitis and the serum sickness syndrome and of little use in asthma

In instances of bone marrow depression resulting from drug allergy particularly agranulocytosis vigorous prophylactic chemothrapy is essential Pencillin procaine should be given in doses of 300 000 units twice a day intramuscularly unless of course penicillin has caused the reaction Then another antibacterial agent such as tetracycline (Achro mycin) 1 to 2 gm daily by mouth should be chosen

In the more protracted and severe cases cortocotropin (ACTH) and cortisone may be used They may be particularly useful in the treatment of exfoliative dermatitis purpura and polyarteritis nodosa The dose of these hormones may be similar to that used for the treatment

7 to 14 days after injection, and should be treated in the same way Bed rest and salicylates for the joint symptoms should be used as outlined under arthritis In the mild cases, frequently that is all that is necessary If urticaria is present also, the oral administration of calcium gluconate or lactate, 1 0 gm 3 or 4 times a day, is very useful With more serious involvement—abdominal pain, diarrhea, lymphadenopathy and even signs of nervous system dysfunction—one of the antihistamines should be tried, either diphenhydramine (Benadryl) hydrochloride, tripelennamine (Pyribenzamine) hydrochloride, or pyrilamine (Neoantergan) maleate in doses ranging from 50 mg 3 times a day to 100 mg 4 times a day depending upon the severity of symptoms

The steroid hormones, cortocotropin (ACTH) or cortisone, may be extremely useful in severe cases, the former in doses of 10 to 25 mg every 6 hours intramuscularly, or 15 to 25 mg dissolved in 1000 cc 5 per cent dextrose solution given slowly intravenously over an 8 hour period, the latter in doses of 100 to 200 mg orally in divided doses daily On the other hand, the steroid hormones should not be relied upon completely in the treatment of serum sickness since the authors have seen several cases in which the hormones not only did not aid in improvement but may have made the condition worse

The prevention of serum sickness may be brought about by careful questioning of the patient concerning previous administration of horse serum, or antitoxins, or even penicillin and, if there is doubt, the testing of the patient for sensitivity as described on page 15 Since there is a quantitative statistical relationship between the amount of serum given and the frequency of resulting serum sickness, no more serum should be given than is necessary to produce the desired results in a given case Although the sulfonamides and antibiotics have largely replaced many sera and antitoxins, antitoxins still hold a very important place in the therapeutic armamentarium against diphtheria, tetanus, snake bite, botulism, and gas gangrene Penicillin is not infrequently the cause of a clinical picture resembling serum sickness

Urticaria

Urticaria, or hives is of either the acute or chronic type The difference is chiefly one of duration, although there are some variations in cause In either type the causative agent should be sought for diligently it is not always allergenic, and often is never found With foods, drugs,

DERMATITIS (CONTACT) *(continued)*

Nupercaine
Opium
Penicillin
Phenolphthalein
Procaine
Streptomycin
Sulfadiazine
Sulfathiazole
Tetracaine (Pontocaine)
Thephorin
Tripelennamine (Pyribenzamine)
Tyrothricin

APLASTIC ANEMIA

Aurothioglucose (Solganal)
Dexedrine
Mapharsen
Mesantoin
Sulfarsphenamine
Sulfathiazole
Trimethadione (Tridione)

THROMBOCYTOPENIC PURPURA

Aurothioglucose (Solganal)
Bismarsen
Gold Calcium Keratinate
Gold Sodium Thiomalate
Gold Sodium Thiosulfate
Iodine tincture of
Neoarsphenamine
Nirvanol
Potassium Iodide
Quinine
Quinidine
Sedormid
Silver Arsphenamine
Sulfadiazine
Sulfapyridine
Sulfarsphenamine
Sulfathiazole

Thiouracil
Thiourea
Triphal

FEVER WITHOUT OTHER ALLERGIC MANIFESTATIONS

Arsphenamine
Neoarsphenamine
Quinidine
Streptomycin
Sulfadiazine
Sulfaguanidine
Sulfapyridine
Sulfathiazole
Thiouracil

AGRANULOCYTOSIS

Aminopyrine
Arsphenamine
Dinitrophenol
Gantrisin
Gold Sodium Thiosulfate
Lopion
Methaphenilene (Diatrin)
Methylthiouracil
Neoarsphenamine
Nirvanol
Oxophenarsine hydrochloride
Presidon
Propylthiouracil
R P 2339
Silver Arsphenamine
Sulfadiazine
Sulfamethylthiazole
Sulfanilamide
Sulfapyridine
Sulfarsphenamine
Sulfathiazole
Thiouracil
Trimethadine (Tridione)
Tripelennamine (Pyribenzamine)

has been stopped It should also be remembered that chemically related drugs can produce a reaction in addition to that caused by original substance Also persons with known eczema, hay fever, or asthma do not appear to be correspondingly likely to become allergic to drugs Finally, topical administration of drugs causes allergic reactions much more frequently than administration by mouth or by injection In the present age as Carr has aptly remarked, the seemingly innocuous jar of penicillin or sulfonamide ointment has become the dermatologist's cask of Amontillado

The manifestations of allergy to drugs include reactions that are also seen in allergy to proteins as asthma, urticaria, angioneurotic edema the syndrome of serum sickness and periarteritis nodosa, dermatitis, and reactions that are not characteristic of allergy to proteins, as bone marrow depression fever that may be unaccompanied by other manifestations of allergy and hepatitis Whatever the manifestations, very often the patient will suggest that he or she does not tolerate certain, or sometimes any medicines well *Always listen to what the patient says concerning intolerance to medicines and do not scoff at it*

The treatment of an allergic reaction to a drug, or drugs, depends upon whether the manifestations are acute and severe or mild and more prolonged

In an acute reaction, which may develop within a few minutes after the drug is administered and usually is characterized by generalized urticaria, angioneurotic edema, asthma, and circulatory collapse, prompt treatment is required The outcome may be fatal, particularly if the drug was given intravenously Give immediately 0 3 to 0 5 cc of 1 1000 epinephrine hydrochloride subcutaneously If the reaction has been very rapid and severe dilute 1 0 cc of 1 1000 epinephrine hydrochloride with 9 0 cc sterile saline and give very slowly intravenously, carefully observing the patient's reaction For more prolonged effect, 1 0 cc of 1 1000 epinephrine hydrochloride may be placed in 500 or 1000 cc of sterile saline and given intravenously If the offending drug has been given subcutaneously or intramuscularly, place ice or a cold object over the injected site and apply a tourniquet to cut off venous return from the extremity The subcutaneous epinephrine mentioned above may be injected at the site to delay absorption of the harmful drug An antihistamine drug such as diphenhydramine (Benadryl) hydrochloride or tripelennamine (Pyribenzamine) hydrochloride 10 to 50 mg may be given intravenously from a syringe or by slow infusion with epinephrine for its anti allergic effects and also because it will potentiate the

A

of other conditions, namely ACTH in an initial dose of 80 to 120 units intramuscularly daily for 3 days, then decreased Cortisone may be begun in doses of 50 mg 4 or 5 times a day, intramuscularly or orally for 3 days, then the dose may be decreased Usually, either agent will not need to be continued for longer than 10 to 14 days

Some drugs are more likely to cause certain types of reactions than others, and the following list, taken from Carr, can be very useful in the study of a specific case

URTICARIA

Acetylsalicylic acid
Arsphenamine
Aureomycin
Cinchophen
Dinitrophenol
Estradiol
Mercurophylline (Mercuzanthin)
Neoarsphenamine
Phenolphthalein
Penicillin
Streptomycin
Sulfobromophthalein

ANGIONEUROTIC EDEMA

Aureomycin
Dinitrophenol
Penicillin
Sulfapyridine

ASTHMA

Acetylsalicylic acid
Meralluride (Mercuhydrin)
Procaine
Streptomycin
Sulfadiazine
Sulfathiazole

DERMATITIS (NOT CONTACT)

Antipyrine
Aureomycin
Dilantin
Dinitrophenol
Neocinchophen
Nirvanol
Penicillin
Phenobarbital
Phenolphthalein
Potassium Iodide
Potassium Thiocyanate
Quinidine
Streptomycin
Sulfadiazine
Sulfanilamide
Sulfapyridine
Sulfathiazole
Thiouracil
Tripelennamine (Pyribenzamine)
Undecylenic Acid

DERMATITIS (CONTACT)

Antazoline (Antistine)
Butamben (Butesin) picrate
Cod liver oil
Dimercaprol (BAL)
Dionine
Intracaine
Iodine tincture of
Larocaine
Merthiolate
Morphine
Neoarsphenamine
Nitrofurazine (Furacin)

Insect (Entomogenous) Allergy

Symptoms of asthma may result from inhalation of insect emanations, particularly from the order Trichoptera, the sand fly or caddis fly, from the order Ephemerida, the May fly, or from the order Lepidoptera, the various moths Occasionally, respiratory symptoms may result from bees, bed bugs and house flies The treatment consists of the use of epinephrine subcutaneously and the antihistamines as outlined under hay fever and asthma In severe cases desensitization with diluted ex tracts of the offending species may be attempted

In the case of biting or sucking insects, such as of the order Diptera biting flies and mosquitoes, the order Hymenoptera, biting ants, the order Siphonoptera, fleas, the order Anophera, sucking lice, and the order Hemiptera, bed bugs and other true bugs, and the stinging insects, of the order Hymenoptera, particularly bees, wasps, and hornets, the individual skin lesions can be greatly alleviated by the oral use of one of the antihistamines diphenhydramine (Benadryl) hydrochloride and tripelennamine (Pyribenzamine) hydrochloride, 50 to 100 mg 3 or 4 times a day In more severe reactions either epinephrine hydrochloride 0 3 cc of 1 1000 subcutaneously, or ephedrine sulfate, 24 mg by mouth, repeated as necessary may be required If an individual is affected fre quently and severely enough desensitization with diluted solutions of extract of the given species may be attempted

BIBLIOGRAPHY

1 WALKER I C 'Hay Fever," *Oxford Med*, vol II, part I, p 245
2 KERN R A and WIMBERLEY N A Penicillin Reactions, *Am Jour Med Sci*, 1953 ccxxvi, p 357
3 CARR E A Jr Allergy to Drugs' *N E J Med*, 1951 ccxlv, pp 892 935
4 LOWELL F C 'The Prevention and Treatment of Drug Allergies *Med Clin No Amer*, Sept 1953 p 1409
5 BROWN E A Drug Allergy, *The Quarterly Review of Allergy and Applied Immunology*, March 1953 vol vii pp 51 82

D

O

P

Q

R

S

X

Y

Z

W

SUPPLEMENTARY INDEX 1